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EDITOR OF THE *British Medical Journal*.

Vol. 4. APRIL, 1929. No. 20.

Medical Lib.

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ISSUED BY THE BRITISH MEDICAL ASSOCIATION.
London: British Medical Association House,
Tavistock Square, W.C.1.

Yearly Subscription (6 numbers), 25/- *Single Number*, 4/6

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A CASE OF PURULENT PERICARDITIS FOLLOWING ACUTE OSTEOMYELITIS.

BY

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The condition of purulent pericarditis is one of considerable interest to the clinician owing to its high mortality, to the difficulty in diagnosis which often attends it, and to the question of treatment, particularly the route of surgical approach.

Frequency. Though not frequently met with clinically, the condition is not a rare one if the comparatively large group of cases which are demonstrated only in the post-mortem room is included. Thus Alexander[1] found only three cases of suppurative pericarditis in 31,016 hospital cases, though Stone[2] noted 15·5 per cent. in 300 patients dead of pneumonia. Allbutt and Rolleston[3] also stressed the frequency with which purulent pericarditis is overlooked in childhood until the post-mortem examination. Poynton[4] investigating 100 autopsies on cases of purulent pericarditis found that only six of these had been diagnosed during life, and considered few conditions more difficult to detect. It is probable, however, that Osler[5], in referring to it as the most commonly overlooked serious disease, had in mind the terminal pericarditis of chronic diseases such as cirrhosis of the liver, diabetes, chronic nephritis, etc.

Ætiology. Purulent pericarditis is, with the single exception of direct trauma (penetrating wounds) with infection, always secondary to some other infective condition. The most frequent causes are pneumonia, empyema, acute specific fevers (measles, scarlet fever, typhoid fever) osteomyelitis, tuberculosis, rheumatism (very rarely, if ever, suppurative).

Coutts[6] distinguishes the commonest types by his statement that a limited number of cases occur in osteomyelitis, whilst practically all the rest have a causal origin in the presence of the pneumococcus.

Diagnosis. Owing to the frequently insidious onset, the diagnosis is often difficult even to one on the look out for the condition, though it is overlooked on occasions owing to the severity of the associated disease. In the majority of cases, however, most, if not all, of the following symptoms and signs will be found to be present.

(1) Pericardial friction rub, it must be admitted, is not an uniformly reliable sign in the suppurative cases. It is frequently absent (Coutts[6], Poynton[4]) or it may be very transitory. In one of the cases reported by Brooke[7] the friction had disappeared within six hours of its appearance. (2) Increased pericardial dullness, this area being pear-shaped and the increase showing itself chiefly in an upward direction so as to occupy the second left intercostal space (as exemplified by the present case), also extending to the

right beyond the right border of the sternum especially in the fifth space (Rotch's sign) and to the left beyond the apex beat. An area of dullness and bronchial breathing at the angle of the left scapula, which is often found in young patients, is due to compression of the lung (Bamberger's sign). (3) Feeble or absent apex beat. (4) Muffled or absent heart sounds. (5) Præcordial bulging in children. (6) Præcordial or epigastric pain. (7) Attacks of dyspnœa. (8) Cyanosis, but also frequently marked pallor. (9) Enlarged heart shadow on X-ray examination. (10) Fluctuating temperature. (11) Leucocytosis. (12) Signs of heart failure (œdema of legs, etc.).

Of these signs the most reliable are (*a*) increased pericardial dullness (*b*) feeble or absent apex beat and heart sounds, and (*c*) enlarged globular heart shadow on X-ray examination.

Considerable difficulty may be met with in differentiating pericardial effusion from cardiac dilatation, though this difficulty will arise less often when the effusion is purulent, as the fluctuating temperature and leucocytosis may be significant.

The points to be kept in mind are the sharp and clear heat sounds in dilatation contrasted with their muffled character in pericarditis, and the fact that compression of the lung is rare in dilatation. The convex right border of the dull area of effusion, as distinct from the straight border in dilatation, which is often described, is of doubtful value.

The question of paracentesis of the pericardium as a diagnostic measure is discussed below.

Prognosis. Purulent pericarditis is a very serious condition, the mortality rate of all types of cases being about 60 per cent. (Appel[8] gives a death-rate of 65 per cent., and Alexander[1] 56 per cent.). The published figures, however, include all cases of purulent effusion and make no distinction between their various causes. There is no doubt that the mortality rate of the cases secondary to acute osteomyelitis is very much higher than that of pneumococcal cases, which, a search of the literature shows, formed a large proportion of the cases which recovered. This group (osteomyelitis) is variously described as being 'desperately dangerous,' 'invariably fatal,' 'usually fatal' (Osler and McCrae[5]), etc.

Shipley and Winslow[9] state that the cases following osteomyelitis are associated with a very bad prognosis, considerably worse than those due to pneumonia, empyema, and penetrating wounds. Brooke[7] collected 36 cases of purulent pericarditis secondary to osteomyelitis in which drainage of the pericardium was performed, including three cases he himself records, with only two recoveries: a mortality of 94 per cent. The reason for this high death rate in the osteomyelitis cases probably depends upon the fact that the pyopericardium results from the rupture into the pericardial cavity of a small metastatic abscess in the heart muscle (*i.e.*, the condition is a pyæmic manifestation), whereas in pneumonia and empyema the infection of the pericardium is due to direct extension to the adjacent serous cavity.

Paracentesis pericardii. The question of the advisability of aspiration of the pericardium as a diagnostic measure is an interesting one and has occasioned considerable discussion.

It must be admitted that as the diagnosis of pericardial effusion is often difficult, any accessory means of verification, both of the effusion and its nature, whether serous or purulent, would be justifiable provided it is free from danger. There is no doubt that tapping the pericardium carries with it a definite risk of puncture of the heart and of the pleura or lung (and thus carrying the infection to the latter structures).

Rowlands[8] confirmed the findings of Sick that the margin of the left pleura nearly always lies under cover of the left border of the sternum at the level of the 5th costal cartilage, and often also at the level of the 6th cartilage, so that in puncturing through the 5th or 6th left spaces, even close to the sternal margin, the pleura must in the majority of cases be traversed. Puncture through the 6th space has the additional disadvantage that the 6th and 7th costal cartilages are often so close together than the space is practically non-existent.

The danger of puncturing the pleura can be avoided by tapping through the left costo-xiphoid angle, the needle being directed inwards and slightly upwards.

Le Conte[10] is of opinion that exploratory puncture is essential in making a diagnosis, whereas Rhodes[11] considers the procedure should be condemned. Coutts[6] was very much averse to paracentesis as he had known a left sided pleurisy result and also seven cases of puncture of the heart, though he admitted with no ill effects. Roberts[12] in 1897 preferred incision and exploration rather than aspiration, but in 1923 considered that the danger of injury to the heart was over-rated and disagreed with Ballance[13] that 'aspiration of the pericardium should be banished as a surgical procedure.'

It would appear to be reasonable to sum up the question as follows :— At the present day, with the aid of good radiograms, the diagnosis of pericardial effusion should be possible with fair certainty ; in the cases where the effusion is secondary to some pyogenic infection it is certain that the fluid will eventually become purulent, so that paracentesis is superfluous and should be replaced by immediate exploration of the pericardium and drainage.

Treatment. Whatever opinions are held about the question of paracentesis as a diagnostic measure, it must be admitted that aspiration has little place in the treatment of a purulent effusion. Free drainage is essential.

There are three main methods of surgical approach to the pericardium : (1) simple incision ; (2) excision of costal cartilage ; (3) the epigastric route.

(1) *Simple incision* through the 5th left intercostal space. The drainage is imperfect, and the pleura and internal mammary vessels difficult to define and avoid through the narrow space.

(2) ***Excision of two inches of the 5th left costal cartilage.*** The pleura and internal mammary vessels can be seen and displaced, but the drainage is anteriorly and not at the most dependent part of the pericardial sac. If

necessary, part of the 6th costal cartilage can be excised in addition, and even part of the sternum nibbled away (especially in children in whom it may still be cartilaginous) in order to gain better access.

The various flap operations, which consist of turning over like a trap-door flaps made up of the whole thickness of the chest wall including one or more costal cartilages, are more applicable to operations on the heart itself (*e.g.*, suture of wounds or removal of foreign bodies) than to drainage of the pericardium.

(3) *The epigastric route.* This method was first devised by Allingham[14] who, in a paper describing a case he had operated on by excising part of the 5th left costal cartilage, suggested a better method of approach through the diaphragm, an incision being made below the left costal margin and the interval between the costal and sternal fibres of the diaphragm defined and incised, and the pericardium then exposed and opened.

He considered that the advantages of this route would be, first, a sure way of entering the pericardium without injuring the pleura; and, secondly, drainage would be from the most dependent part of the sac if the patient were half propped up and would be through a large opening not bounded by cartilages or sternum. He considered that this method would be particularly applicable to children with flexible cartilages (so enabling the left costal margin to be retracted if necessary in order to improve the exposure). In adults with rigid cartilages it would be better to excise two inches of the 7th costal cartilage in addition.

Rowlands[6] brought forward the following criticisms:—(1) The little room available in adults with rigid or ossified cartilages. This objection is met by Allingham's suggestion of excising part of the 7th costal cartilage (and even of the 6th) when necessary. (2) The operation is necessarily performed somewhat in the dark and under cover of the sternum and 7th costal cartilage, and the operator may not be certain whether the exploring finger is above or below the diaphragm so that the peritoneum may be opened. (3) The pericardium may be separated by the finger from the parietes, and pus may leak into the loose connective tissue and set up a fatal mediastinitis. He admits that the operation would be easier in children, owing to the elasticity of the boundaries of the costo-xiphoid angle.

In the case described below this method of exposure was used and the writer found no difficulty in defining and displacing the peritoneum downwards, and there appeared surprisingly little danger of opening it: moreover, the bulging pericardial wall could be easily felt after the costo-xiphoid space had been opened, so that there was little likelihood of separating it from the parietes and so opening up the mediastinal space. It would, therefore, appear that the above criticisms are not entirely justified.

The drainage obtained in this patient, when she was propped up in a half-sitting position, was entirely satisfactory.

To summarize, simple incision allows such imperfect drainage that it should be confined to desperate cases where very limited surgery only is justifiable. Excision of parts of the 5th and, if necessary, 6th costal cartilages gives good exposure, but the drainage is not entirely satisfactory. The epigastric route is the method of choice in children, but may be difficult and the exposure restricted, in adult patients.

It should be noted that local anæsthesia would allow of the performance of either of the two last operations, even in very ill patients, with comparatively little disturbance.

Case Report.

A female child, aged 4 years and 10 months, was admitted to St. Bartholomew's Hospital on October 7th, 1928, with the history that at 3 o'clock that morning she woke up with sudden agonizing pain in the left thigh, together with signs of septic intoxication—hectic flush, sweating and continuing delirium.

On admission, 3 p.m., October 7th (*i.e.*, 12 hours after the onset of symptoms), her condition was as follows:—

Looked very ill and toxæmic. Marked hectic flush, delirious with intermittent spasmodic movements of whole body. Temp. 104°. Pulse 130. Respiration 28.

The left knee was held flexed and the child jumped in agony if the left thigh—especially the lower part—was touched. The general outline of the thigh was swollen and the skin a little reddened just above the internal condyle. No definite lump was palpable. There was no effusion in the knee joint.

Heart and lungs showed no abnormality. Urine, specimen not obtained (patient incontinent).

The diagnosis of acute osteomyelitis of the femur was made, and immediate operation carried out.

Operation (*October 7th*).—Under gas, oxygen, and ether an incision was made over the internal aspect of the lower end of the femur for 3 in. upwards from the adductor tubercle and deepened down to the periosteum which was found to be raised from the bone by a subperiosteal collection of thin, blood-stained pus, which was evacuated. No opening into the medulla was found. A gutter was made into the bone at the level of the epiphyseal line and drainage tubes inserted. Unfortunately the pus was not examined bacteriologically, but there can be little doubt that it was staphylococcal in origin.

Her condition remained about the same until the 4th day (October 12th) when the respiration rate shot up to 80, she became cyanosed, and signs of broncho-pneumonia, involving both lungs, became manifest. By the 18th October (12th day of illness) the temperature had fallen by lysis to normal but the pulse rate, which since admission had remained about 150 to 160, showed no diminution in rate, while the respiration rate had dropped to about 45. Her general condition had improved, she was quite rational and more amenable to treatment. During this time the wound had been discharging satisfactorily and the swelling of the thigh had subsided.

For the next nine days (October 18th—26th) the improvement in her condition was maintained, the temperature being about normal (with a rise to 100° on four occasions), the lung signs clearing up except for some scattered râles, and the patient less fretful and taking nourishment well, but the slight cyanosis persisted and the pulse and respiration rates still remained high (about 150 and 45 respectively) though the pulse was of good volume.

On October 26th (20th day of the illness) her temperature was 100°, pulse 150, and respirations 50. During the course of routine examination an area of impaired respiratory movement and of dullness appeared in the upper part of the front of the chest on the left side in the second intercostal space, but at this time this area of dullness was not demonstrated to be continuous with the cardiac dullness which was not increased to the right or to the left; there was no præcordial bulge.

From this date the temperature became intermittent in character, varying between 97·4° and 102°, the pulse rate showing similar variations. This suggested the presence of suppuration, which was confirmed by a leucocyte count of 23,800 on November 1st. The local condition was quite satisfactory and did not appear to account for this temperature and leucocytosis.

November 1st.—Temp. 102°. Pulse 156. Resp. 60. Definite impaired movement and dullness of the left chest anteriorly up to the level of the second rib.

Apex beat not palpable. No præcordial bulge. Area of cardiac dullness: above, 2nd rib; to right, ¾-in. to R. of sternum; to left, 1 in. outside mid-clavicular line. On auscultation: no heart sounds audible. No pericardial friction heard.

Dr. Graham saw the patient and diagnosed pericardial effusion, probably purulent. The presence of this effusion was confirmed by X-ray examination (see Fig. 1) X-ray report:—'The heart shadow is enormously enlarged in all directions, especially upwards, and has assumed the typical rounded appearance associated with pericardial effusion. There is also some thickening of the pleura at the base of the left lung.'

Operation (*November 2nd*).—Exploration of pericardium. Under gas and oxygen anæsthesia, and without previous aspiration, a vertical incision was made below the costal margin ¾ in. to the left of the mid-line, separating the fibres of the left rectus muscle. The peritoneum was exposed and pushed downwards, the tissue between the sternal and costal fibres of the diaphragm separated and the pericardium incised. Immediately between 12 and 14 ounces of slightly turbid fluid gushed out under considerable tension. A specimen was taken for bacteriological investigation. The forefinger was inserted into the cavity and the heart felt beating strongly; no adhesions could be felt.

As the fluid was only slightly turbid it was not thought justifiable, owing to the risk of secondary infection, to insert a drainage tube into the pericardial cavity until the bacteriology of the fluid was known; the wound was accordingly closed without drainage.

Bacteriological report of pericardial fluid: A slightly turbid fluid, Gram-stained films of which showed large numbers of polymorph leucocytes but no organisms. Cultures on blood-legumen-agar showed a fair growth of staphylococcus aureus.

Second Operation (*November 3rd*).—In view of the culture report (showing organisms to be present in the pericardial fluid) under ethyl chloride anæsthesia the wound was rapidly re-opened, an ounce of two of fluid, more turbid than on the previous day, was evacuated and a drainage tube inserted just into the pericardium through the opening previously made in it.

After the operation the wound drained freely, the discharge by the following day consisting of frank pus, while the patient's general condition improved slightly and the temperature fell gradually to normal by the fourth day.

The area of pericardial dullness diminished at once so as to reach upwards only as far as the third rib.

The pericardium was irrigated on the 2nd, 3rd, and 4th days, but as only a few flakes of fibrin came away this procedure was not repeated. The drainage tube was removed on the 10th day and the wound had almost healed up 6 days later.

November 6th.—Blood count:—R.B.C. = 4,860,000. W.B.C. = 15,400. Hæmoglobin = 77%. Colour index = 0·8.

About this time, however (November 7th) the region of the left axilla showed, on daily examination, an increasing impairment of movement and percussion note, with the appearance of pleural rub; and on aspiration in the 8th space in the posterior axillary line 3 to 4 c.cm of pus was withdrawn. Cultures of the pus showed a pure growth of staphylococcus aureus.

Operation (*November 9th*).—In view of this 1½ in. of the 8th rib in the posterior axillary line was resected under local anæsthesia but no pus was found on opening the pleural cavity; the visceral layer was, however, thickened and adherent to the parietal layer. These recent adhesions were gently separated in an upward direction but no purulent collection was discovered. A needle was introduced into the lung substance for 1½ in., but no pus was withdrawn. A drainage tube was inserted and the wound partially closed. The pleural thickening which was found at this operation had been noted in the X-ray report of November 2nd.

After this operation the temperature continued irregular for four days, but from then onwards remained about normal with occasional rises to 100°. The patient's general condition improved steadily for a time, but on November 20th signs of heart failure, œdema of legs, back

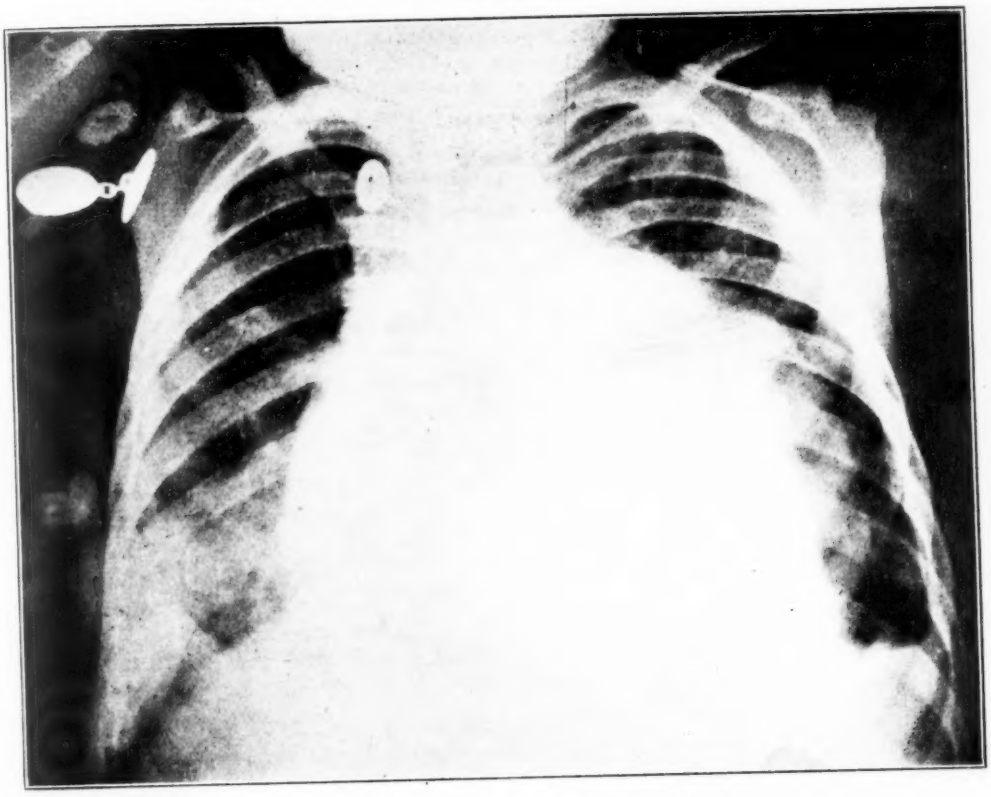

Fig. 1. Skiagram of chest before operation.

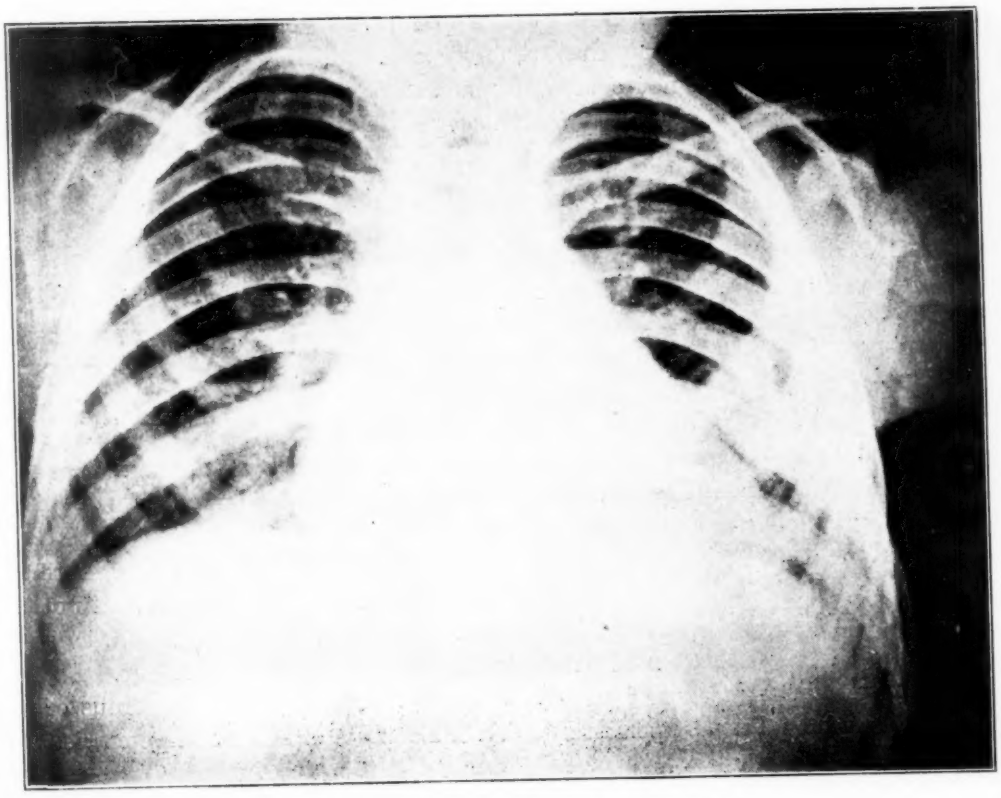

Fig. 2. Skiagram of chest after operation

and abdominal wall with signs of ascites, appeared, the swelling of the abdomen being especially marked in the right flank where a definite tumour was felt.

On November 28th, the general condition of the patient not being satisfactory and the question of re-accumulation of pus in the pericardium being considered, exploration of the pericardium through the original wound was carried out but no purulent collection was found. At the same time the swelling in the right loin was investigated by aspiration, straw coloured ascitic fluid being withdrawn; and the second left intercostal space aspirated (there being in view of persistent dullness in this region the possibility of empyema) but no pus was found.

On November 30th paracentesis abdominis was performed and 36 oz. of ascitic fluid removed.

Following the paracentesis the œdema very rapidly disappeared and the patient's general condition improved steadily, the temperature during this time remaining about normal, the pulse rate gradually diminishing to 120 and the respiration rate to 30.

The patient was up for the first time on January 1st, 1929, and was discharged to a Convalescent home on January 15th.

Clinical examination just before discharge showed the apex beat to be in the 5th space in the nipple line. The area of cardiac dullness was above, 3rd rib; to right, at the right border of sternum, and to left at the apex beat. Heart sounds natural. Apex beat does not move on turning the patient. The pleural, pericardial, and thigh wounds had healed and there was no ascites or enlargement of the liver.

An X-ray examination of the chest (see Fig. 2) was reported on as follows:—'A portion of the 8th left rib has been removed and has reformed. The heart shadow is still enlarged. This enlargement extends right up to the aorta. It has not, however, the typical globular appearance of pericardial effusion, which was previously seen, but is now pear-shaped. The width of the aorta suggests pericardial thickening or a little effusion.

Discussion.

This case presented several interesting features. The onset of the purulent pericarditis was insidious, as is usual in these cases, and it is probable that the effusion had been present for some days before it was diagnosed. The area of dullness in the 2nd left intercostal space was noted six days before, but its significance was not at that time appreciated, the previous bronchopneumonia, which had not completely subsided, rather confusing the issue. No pericardial friction was heard but this sign, which is inconstant and often transitory, may easily have been overlooked.

With regard to the symptoms, these were certainly not classical.

The child did not look gravely ill; indeed, her condition was very different from that during the first week. She was only slightly cyanosed, and the pallor, anxious expression and præcordial pain, which are often described as prominent features, were absent. She had for some days a short irritating cough which was considered to be due to the lung condition, whereas it was probably reflex.

The diagnosis was made on the following physical signs—increased pericardial dullness (confirmed by the radiogram); absent apex beat and heart sounds with a persistent rapid pulse, together with signs of suppuration, *i.e.*, fluctuating temperature and leucocytosis.

In reference to the operation of pericardial exploration in this case there is no doubt that a drainage tube should have been inserted at once, and not delayed for 24 hours to await the result of bacteriological examination, as a pericardial effusion in cases of osteomyelitis always becomes purulent. For the same reason aspiration of an effusion in such a case while still serous or seropurulent should not be performed, but immediate and free drainage carried out.

One point in the after treatment demands mention, namely, the question of irrigation of the pericardial cavity. In this case gentle lavage with saline solution was carried out on the second, third, and fourth days without any untoward result, but as little more than a few shreds came away and the drainage was satisfactory it was not continued. There is a danger, during lavage, if a free outlet for the irrigating fluid is not maintained, for the intra-pericardial pressure to increase so much as to embarrass the action of the heart with sudden fatal consequences.

Another of the more interesting points in the case is the question of the situation of the pus which was removed presumably from the left pleural cavity by aspiration in the 8th space, but which the subsequent operation for empyema failed to locate.

The possibilities are, first, that the 3 or 4 c.cm. of pus removed by needling represented the whole of the contents of a very small empyema which was completely evacuated by the aspiration. This is the most probable explanation, for the needle was only inserted far enough to enter the pleural cavity when pus was obtained ; moreover, the thickening of both visceral and parietal pleura and their recent adhesions demonstrated at operation, afforded confirmatory evidence of this. Secondly, that a small lung abscess, and not a collection in the pleural cavity, had been tapped. Against this possibility is the fact that at the subsequent operation when no pus was found, the lung was needled to a depth of $\frac{3}{4}$-inch in several places. Thirdly, that the pus was aspirated from the pericardium. Though the pericardium, before it was drained, was enormously distended and might easily have been reached by needling from the lateral chest wall, yet after drainage it had collapsed and must have receded too far to be reached by a needle which was only inserted such a short distance.

The last point of interest which should be mentioned is the very marked and rapid improvement which resulted from paracentesis abdominis when ascites developed in the later stages of the illness.

My thanks are due to Mr. Geoffrey Keynes for allowing me to make use of the notes of this case.

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THE LÆVULOSE TEST IN RHEUMATIC AND CHOREIC CHILDREN.*

BY

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In a paper recently published in THE ARCHIVES OF DISEASE IN CHILDHOOD Taylor Chadwick[1] gave the results of an investigation of the behaviour of the lævulose test in the rheumatic child. From the results he concluded that in certain stages of the rheumatic infection the efficiency of the liver is impaired, and he expressed the opinion that this might be due to the result of toxic absorption from some rheumatic focus. In children completely recovered from rheumatism, and in those suffering from uncomplicated chorea, he found that the ingestion of lævulose gave a blood-sugar curve not differing from that obtained in the normal individual. In children presenting active rheumatism, with or without heart affection, and in the examples of chorea with evidence of carditis there was, on the other hand, an appreciable intolerance to lævulose as indicated by a rise in the blood sugar. This rise in the blood sugar varied between 18 per cent. and 113 per cent., with an average increase of 49 per cent.

A survey of the details in Chadwick's paper raises a suspicion that the diminished hepatic efficiency as indicated by the lævulose test is dependent on passive congestion of the liver secondary to cardiac involvement rather than on some toxic action. Of the number of cases in which there was cardiac involvement 54 per cent. reacted abnormally to lævulose. If, however, there be excluded the five cases (Nos. 12, 16, 30, 31 and 34), in which the cardiac involvement was admittedly transient, then the percentage of abnormal findings in Chadwick's cardiac cases rises to 73. On the other hand, of the four rheumatic cases without apparent heart disease, only one (No. 11) gave an abnormal curve. In the text of his paper Chadwick drew attention to the cases with and without heart disease, and while he remarked that the abnormal blood-sugar curve following lævulose bears no relationship to the valvular lesion, he admitted that it did bear a certain relationship to the state of tone of the cardiac muscle. It is, therefore, difficult to appreciate on what grounds he bases his ultimate conclusion that active rheumatism, with or without heart disease, is accompanied by an abnormal blood-sugar curve after the ingestion of lævulose.

In a previous communication[2], also published in this Journal, I recorded the results of a study of the value of the lævulose test as an index of efficiency of the liver. I concluded that a rise of 30 per cent. in the blood-sugar content after the administration of lævulose should be considered as evidence of hepatic

*The work was carried out under a grant from the Medical Research Council

disease, but that wide variations below that figure occur in the normal child. Three of my control cases employed were children who had recently passed through an attack of rheumatic fever, but who had escaped any apparent cardiac involvement. In none of these cases was there any evidence of hepatic inefficiency. In one case of rheumatism with severe valvular disease of the heart and enlargement of the liver, there was found evidence of hepatic inefficiency; the increase in the blood sugar after the ingestion of lævulose amounted on two occasions to 42 per cent. and 43 per cent. respectively, which is well above the upper limit (30 per cent.) of the normal.

Present Investigations.

The following work was undertaken to investigate further the results of the lævulose test in a series of rheumatic and choreic children. As far as can be ascertained from a review of the case histories the type of patient investigated was the same as in Chadwick's series.

Maclean's method for estimating the blood-sugar content was employed throughout; 20 to 30 grm. of Merck's pure lævulose, dissolved in 150 c.cm. of water, were administered *per os*, the amount depending on the age of the child. The blood-sugar estimations were made at half-hourly intervals after the ingestion of the lævulose until the blood sugar had returned to the normal fasting level. The importance of using the purest lævulose was noted in my previous paper.

In the grouping of the cases the same classification as was adopted by Taylor Chadwick was employed, but for better evaluation of the various phases of the rheumatic infection in producing the intolerance to lævulose, some of the groups have been further sub-divided.

Group I.—Rheumatic arthritis without cardiac involvement. (Table I).

Unfortunately I was only able to obtain one case which could be placed in this group. Thirteen days before the test was first performed this child had taken ill with fever, rapid pulse and pains in the hips, knees and wrists which persisted for nine days. For six days before the test the child had been on sodium salicylate, and for four days there had been no pain in any of the joints, and the temperature and pulse had remained normal. At this time there was a rise in the blood sugar of 32 per cent., which is slightly above the highest normal figure. The temperature and pulse remained within normal limits and there was no further complaint of any joint pains; and three weeks still later, when the test was repeated, no rise in the blood sugar was obtained. The interesting point in this case is that a higher rise was obtained when the infection was more active than during convalescence.

Group II.—Convalescent rheumatic arthritis with cardiac involvement.

This group, the details of which are given in Tables II, III, and IV, has been subdivided into (*a*) cases where the cardiac murmur was transient; (*b*) cases where there was definite cardiac disease but no signs of incompetency; and (*c*) cases of severe cardiac disease with incompetence.

(*a*) In considering the cases where the cardiac murmur was transient and there was no evidence of active rheumatic arthritis, one (No. 2) gave a definite rise in the blood sugar of 43 per cent., while the other (No. 3), gave only a rise of 7 per cent. Unfortunately a repeat test was not possible in Case 2, as the child vomited after the second dose of lævulose. (Table II).

(*b*) Of the twelve examples of convalescent rheumatism with cardiac disease, none showed any abnormality in the behaviour of the blood sugar after the ingestion of lævulose. (Table III).

(*c*) There were five cases with severe cardiac disease and some degree of incompetence, and two (Nos. 18 and 20) showed a definite rise in the blood sugar of 92 per cent. and 37 per cent. respectively. No. 18 also showed a delay in the return to the normal fasting level. This was a very severe case of cardiac failure with œdema of the feet and enlargement of the liver, in which an abnormal lævulose reaction was not unexpected. In another case (No. 20) the child appeared on clinical examination to be in the same state at the time of both tests, yet at the first examination a rise of 37 per cent. was obtained, while six days later the blood sugar remained practically level for two hours after the ingestion of the lævulose. (Table IV).

Group III.—Active chorea without cardiac involvement. (Table V).

In the five cases of this group in which the chorea was still active but in which there was no evidence of any involvement of the heart, two (Nos. 22 and 23), as seen in Table V, responded with a definite rise in the blood sugar of 40 per cent. and 45 per cent. respectively. In the other three cases the blood-sugar curve was normal. A repeat test was performed in one of them (No. 23) one month later when the chorea was less marked, but the rise obtained in the blood sugar was well within the limits of experimental error.

Group IV.—Active chorea with cardiac involvement. (Table VI).

This group consisted of twelve cases of active chorea with definite evidence of cardiac involvement, although in none was the cardiac disease very severe. Only two of these cases (Nos. 27 and 36) gave a definite rise in the blood sugar, an increase of 54 per cent. and 45 per cent. respectively being obtained. Repeat tests were performed in each, but no rise in the blood sugar was obtained in either on the subsequent occasions. In Case 36 there was definite improvement clinically at the time of the second examination, all the chorea having disappeared although the heart condition remained the same. Case 27, on clinical examination, appeared to be in the same condition on all three occasions.

Group V.—Convalescent chorea without cardiac involvement. (Table VII).

Three children (Nos. 38, 39 and 40) were examined a short time after all choreic movements had disappeared, and as is seen in Table VII, in none was there any definite increase in the blood sugar after the ingestion of the lævulose.

Group VI.—Convalescent chorea with definite cardiac disease. (Table VIII).

There are three cases (Nos. 41, 42 and 36, the last at the time of the second examination) which may be considered under this heading. Although the

children had a definite heart lesion all the choreic movements had disappeared, and as in the case of convalescent chorea without any heart involvement, there was no evidence of any hepatic inefficiency as shown by the lævulose test.

Discussion.

From a general survey of the results (Table IX) in these various groups of rheumatic cases, it is impossible to appreciate any consistent behaviour towards lævulose during any one phase of the disease unless it be that convalescent chorea invariably reacts as in health, a normal curve always being obtained. The number in this group is, however, small, namely, six, and one does not therefore wish to draw far-reaching conclusions.

Contrary to expectations, cardiac disease, at least valvular disease, is not the determining factor, since of the total cases with heart involvement 12 per cent. reacted abnormally, whereas of those without heart disease 33 per cent. reacted abnormally. In this latter group again, however, the number is small, namely, nine.

It is, of course, the condition of the myocardium which is of moment in this connection, and it is just this factor which is most difficult to estimate. Cardiac disease was diagnosed in the above cases on the presence of a murmur which, as is well known, may be a prominent sign even though the myocardium is quite efficient.

With the idea that the pulse rate would be a better gauge of the efficiency of the myocardium an attempt was made to correlate this with the lævulose test but without success. Of 26 cases with a pulse rate ranging from 70 to 90 per minute, 5 (20 per cent.), reacted pathologically; of 9 cases in which the pulse ranged between 90 and 100, only 1 (10 per cent.), reacted abnormally, and of 15 cases in which the pulse varied between 100 and 120 per minute, only 2 (12 per cent.), gave a rise in the blood sugar after lævulose of more than 30 per cent.

The group which gave the largest proportion of pathological results was that of active chorea, and again the larger proportion of abnormal results was obtained when no cardiac disease was apparent. It is just possible that in chorea there may result overstimulation of the sympathetic nervous system with a consequent disturbance of carbohydrate metabolism.

These findings, it is seen, are very different from those obtained by Taylor Chadwick in his series of cases, and it is difficult to account for such discrepancies. It may be that the efficiency of the liver varies from time to time even in the normal individual, and that two small groups of cases, as undoubtedly both Chadwick's and mine are, will contain in very varying proportions these varying degrees of efficiency.

It is interesting that only one case in my series revealed, in addition to an abnormal rise in the level of the blood sugar, a delayed fall to the fasting level. In this case there was both clinical and pathological evidence of liver derangement (enlargement and passive congestion), and thus in gauging hepatic efficiency it might be advisable to consider not only the percentage rise, but the time taken for the normal level to be regained. In my previous communication

on the lævulose test 76 per cent. of the 25 cases with definite hepatic disease showed an abnormal rise of the blood sugar, and of these 25, 60 per cent. presented a delayed fall. In 11 cases of probable hepatic disease an abnormal rise was obtained in 54 per cent., but in only 18 per cent. of these was there a delayed fall, while in 9 cases of problematical liver disease only 1 case showed an abnormal rise with also a delayed fall, and in 20 normal children none presented a rise of more than 30 per cent., and in no instance a delayed fall.

Conclusions.

1. The lævulose test was performed in 19 children who were suffering from convalescent rheumatic fever with definite cardiac involvement, and of these only 3 gave a rise in the blood sugar of more than 30 per cent. after the ingestion of lævulose.

2. One case of severe cardiac disease with definite clinical and pathological evidence of liver derangement, showed in addition to an abnormal rise in the blood sugar a delay in return to the fasting level.

3. Of 5 cases of active chorea in which there was no evidence of cardiac involvement, two gave a rise in the blood-sugar content of more than 30 per cent. after the ingestion of lævulose: and of 12 cases of active chorea with definite cardiac disease, 2 gave an abnormal rise of blood sugar after the ingestion of lævulose.

4. In 6 cases of convalescent chorea, 3 of which showed evidence of cardiac disease, a normal blood-sugar curve was obtained.

5. Of 32 cases of rheumatic cardiac disease only 4 (12 per cent.) showed an abnormal rise after the ingestion of lævulose; whereas of 9 cases of the rheumatic infection without heart disease, 3 (33 per cent.) showed an increase in the blood sugar of more than 30 per cent.

6. The lævulose test gives no consistent evidence of liver derangement in the rheumatic infection.

(*For Tables see pages* 81 *and* 82.)

References.

1. Chadwick, R. T., *Arch. Dis. Child.*, Lond., 1928, III, 179.
2. Brown, M. J., *Ibid.*, 1928, III, 81.

TABLES I—VI.

THE LÆVULOSE TEST IN RHEUMATIC AND CHOREIC CHILDREN.

Case No.	Repeat after:	Percentage of Sugar in Blood.					
		Fasting.	Hours after lævulose.				Percentage Increase.
			½	1	1½	2	
TABLE I.—*Rheumatic arthritis without a heart lesion.*							
1	———	·068	·068	·090	·086	·070	32
1	3 weeks	·112	·106	·100	·100	—	—
TABLE II.—*Rheumatic arthritis with slight cardiac involvement.*							
2	—	·085	·122	·109	·113	·094	43
3	—	·093	·100	·093	·086	—	7
TABLE III.—*Rheumatic arthritis with definite cardiac disease.*							
4	—	·131	·131	·118	·118	·125	*nil.*
5	—	·100	·098	·093	·100	—	*nil.*
6	—	·125	·112	·118	·125	—	*nil.*
7	—	·112	·125	·112	·106	·106	5
8	—	·093	·086	·090	·081	—	*nil.*
9	—	·112	·143	·112	·131	·112	27
10	—	·125	·112	·118	·118	·131	5
11	—	·093	·098	·081	·098	·093	5
12	—	·081	·086	·086	·075	·081	*nil.*
13	—	·104	·113	·117	·113	·109	12
14	—	·095	·090	·112	·106	·105	18
15	—	·117	·137	·137	·137	·109	17
TABLE IV.—*Rheumatic arthritis with severe cardiac disease.*							
16	—	·125	·135	·118	·118	·125	8
17	—	·118	·081	·112	·084	—	*nil.*
18	—	·081	·106	·143	·156	·143	92
19	—	·081	·086	·070	·086	—	*nil.*
20	—	·068	·061	·090	·086	·070	37
20	6 days	·098	·093	·098	·093	·086	*nil.*
TABLE V.—*Active chorea without any cardiac involvement.*							
21	—	·090	·102	·104	·085	·085	15
22	—	·075	·106	·086	·106	·081	40
23	—	·086	·093	·125	·112	·112	45
23	1 month	·090	·100	·090	·100	·105	15
24	—	·075	·086	·075	·081	—	14
25	—	·097	·114	·093	·084	—	17
TABLE VI.—*Active chorea with cardiac involvement.*							
26	—	·118	·100	·136	·106	·100	15
27	—	·100	·154	·129	·117	·109	54
27	2 weeks	·100	·104	·090	·106	·087	4
27	19 days	·095	·109	·100	·100	·085	15
28	—	·100	·100	·098	·106	—	6
29	—	·093	·112	·106	·093	—	20
30	—	·117	·122	·149	·134	·129	27
31	—	·112	·100	·106	·112	—	*nil.*
32	—	·100	·109	·094	·089	—	9
33	—	·086	·106	·093	·081	·093	23
34	—	·112	·110	·110	·112	—	*nil.*
35	—	·118	·112	·137	·125	·118	15
36	—	·068	·081	·100	·086	·075	45
36	2 weeks	·129	·162	·147	·147	·137	20
37	—	·111	·131	·125	·112	·100	18

TABLES VII. AND VIII.

THE LÆVULOSE TEST IN RHEUMATIC AND CHOREIC CHILDREN.

Case No.	Repeat after:	Percentage of Sugar in Blood.					
		Fasting.	Hours after lævulose.				Percentage Increase.
			½	1	1½	2	
TABLE VII.—*Convalescent chorea without cardiac involvement.*							
38	—	·094	·094	·109	·097	·094	15
39	—	·081	·100	·089	·072	—	20
40	—	·086	·086	·081	·090	—	*nil.*
TABLE VIII.—*Convalescent chorea with cardiac disease.*							
41	—	·093	·085	·085	·085	—	*nil.*
42	—	·082	·082	·077	·082	·077	5
42	5 weeks	·088	·094	·094	·088	—	7
36 (2nd test)	—	·129	·162	·147	·147	·137	20

TABLE IX.

SUMMARY OF RESULTS.

	Total No.	No. of positive lævulose tests.	Percentage of positive lævulose tests.
Cases with heart involvement	32	4	12
Cases without heart involvement	9	3	33
Cases of convalescent arthritis	20	4	20
Cases of convalescent arthritis with heart involvement ...	19	3	16
Cases of convalescent arthritis without heart involvement	1	1	100
Cases of active chorea	17	4	25
Cases of active chorea with heart involvement ...	12	2	16
Cases of active chorea without heart involvement ...	5	2	40
Cases of convalescent chorea	6	0	0
Cases of convalescent chorea with heart involvement ...	3	0	0
Cases of convalescent chorea without heart involvement	3	0	0
Cases of chorea with heart involvement	15	2	13
Cases of chorea without heart involvement	8	2	25

STUDIES OF PNEUMONIA IN CHILDHOOD.

II. ALVEOLAR (LOBAR) PNEUMONIA.

BY

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In the first paper of the series, a statistical analysis of pneumonia and bronchitis in childhood was presented, based on two series of cases, clinical and post-mortem. These were reviewed and classified into various types. The present paper deals with that type of pneumonia usually called lobar, giving a general account of its morbid anatomy and histology, and a report of three cases. It is advisable to explain that we use the term 'alveolar' instead of 'lobar' to designate this type of pneumonia. The reasons for this preference have been given in the preceding paper and will again be alluded to in the course of this paper.

After Barthez and Rilliet had clearly differentiated the type broncho pneumonia in infants and young children, its great frequency was established, and the view was held by many that at this early period of life croupous or lobar pneumonia scarcely ever occurred. Thus Gairdner[1] in 1853 referred to this controversy on the relative frequency of lobular and lobar pneumonia in early childhood in the following passage :—

> Some of the earliest writers on the subject distinctly state that of the two forms of pneumonia, the lobular and the lobar, the former *alone* is to be found in early infancy, the latter *alone* beyond that age. The latest authorities, in some instances at least, will be found to maintain the same opinion, and notwithstanding the distinct observations of Barthez and Rilliet, Legendre and Bailly, Friendleben and others as to the occurrence of *lobar* hepatization in young infants. . . .

In 1888 Henoch[2] summed up the prevailing contemporary view of the controversy as follows :—

> Although catarrhal or broncho-pneumonia is the commonest inflammatory affection of the lung in childhood, yet the view which formerly obtained as to the rareness of the croupous form has long been done away with, and rightly too. Between the third and the twelfth years this disease is indeed very common, and also in the first two years of life it is by no means rare.

The weight of clinical opinion at the present day seems to take the same view. Table I shows the relative numbers of cases of alveolar (croupous, lobar) pneumonia occurring in childhood before and after two years as reported by various authors.

TABLE I.
ALVEOLAR (LOBAR) PNEUMONIA.

Author.	Date.	No. of cases.	No. under 2 yrs.	Percentage under 2 yrs.
Coutts[3]	1902	86	43	50%
Dunlop[4]	1907	147	45	30·5%
Hutchison[5]	1926	70	35	50%
McNeil, Macgregor, and Alexander[6]	1929	386	164	45·2%

These views, old and new, are, however, largely based on clinical diagnosis, corrected to some extent by post-mortem evidence. In a recent discussion on the subject, Findlay[7] strongly reasserted the old doctrine. He maintained that practically all cases of primary pneumonia under the age of three years belonged to the type broncho-pneumonia and based this statement on the evidence of 65 consecutive autopsies of pneumonia in children. In a recent number of this journal, Olive Somerville[8] has published a detailed analysis of this post-mortem material. Out of the total, only one typical lobar pneumonia was found and that in a child aged five years. There were two other cases, both in children under two years, which might be classed as lobar pneumonia but which presented atypical features. The principal criterion of diagnosis in this investigation was the microscopic examination of relatively small pieces of lung tissue.

Although the question in dispute cannot be completely settled by post-mortem evidence, Findlay's results, if confirmed, would go far to overthrow this long preponderant view that alveolar or lobar pneumonia occurs throughout childhood and is fairly common even in infancy. We therefore present a series of fatal cases of alveolar (lobar) pneumonia, the majority of them in children under two years, in which the post-mortem appearances are described, and in which we offer macroscopic and microscopic evidence in justification of the diagnosis of this type of pneumonia.

PATHOLOGICAL STUDY.

Alveolar (lobar) pneumonia is comparatively seldom seen in the post-mortem room of a children's hospital. In uncomplicated cases the mortality is low. The cases which come to autopsy are, as a general rule, those of unusual extent or severity, those in which some dangerous complication has developed, or those in which some pre-existent abnormality has prejudiced the patient's chances of survival. Opportunities of studying the pathology of this disease in straightforward uncomplicated cases of the kind which usually recover are therefore relatively few. This fact occasions some difficulty in determining exactly what are the usual pathological characters of alveolar pneumonia in childhood and infancy, and is responsible for the uncertainty concerning the frequency of this type.

In our previous paper[1] it was stated that of a series of 945 autopsies in cases of death from all causes performed in the Royal Edinburgh Hospital for Sick Children during the period from July, 1922, to October, 1928, inclusive, 23 (2·5 per cent.) were cases of alveolar pneumonia, and 140 (14·8 per cent.) were cases of broncho-pneumonia. There were also examples of other types, the characters and number of which were stated. A short survey of these 23 cases of alveolar pneumonia may be of some interest as an introduction to a study of the morbid anatomy and histology of this type.

Age.—The ages of the children ranged from 4 months to 4 years and 9 months. Twelve were under one year old ; six were between one and two years. Thus more than three-quarters of all the cases were in children under two years of age.

Sex.—There were seventeen boys and six girls. Although the number of cases is far too small to warrant any drawing of conclusions with regard to sex incidence, the preponderance of males is striking, and is in agreement with the figures derived from a much larger series of clinical cases which was reviewed in our previous paper.

Complications.—The incidence of serious complications was very high in this series. In 15 of the 23 cases the pneumonia was accompanied by some complicating condition (either resulting directly from the pneumonic infection or pre-existent), which greatly increased the gravity of the illness, and was in some instances certainly the actual cause of death.

The nature and frequency of these complications were as follows :— empyema, 8 ; pericarditis, 3 ; meningitis, 3 ; abscess in lung, 3 ; peritonitis, 1 ; acute nephritis, 1 ; suppurative pyelonephritis, 1 ; congenital defect of the heart, 1.

Morbid Anatomy.

Site and extent of consolidation.—In 8 of the 23 cases, the right lung only was affected ; in 8, the left lung only ; in 7, both lungs were involved.

In 10 cases, the pneumonia was confined to one lobe. In 13 cases, more than one lobe was wholly or partly consolidated. The order of frequency with which the various lobes were affected was as follows :—left lower lobe, 13 right upper lobe, 9 ; right lower lobe, 8 ; left upper lobe, 5 ; right middle lobe, 4.

In ten cases the area of consolidation extended to one whole lobe or more. In eight cases the pneumonia was present in a single patch the extent of which was less than one lobe. In the remaining five cases, pneumonia was present in more than one lobe, but affected only a part of each. In no case was an entire lung consolidated, although there were instances in which the unaffected part was very small (Plate II, Fig. 5).

In those cases in which the pneumonic area was less than a whole lobe, it was, as a general rule, of considerable size, often about half a lobe (Plate II, Fig. 6) ; but in certain instances no more than a patch about an inch in diameter was consolidated (Plate II, Fig. 7).

When consolidation affected only a part of a lobe, its position in the lobe was very variable. It was more often posterior than anterior. It very seldom failed to reach the pleural surface at some point. In two cases it was situated deeply near the root, without having extended to the surface. Sometimes its position was peripheral, so that it did not approach the root (Plate II, Fig. 7.)

It is evident from these observations that, although this disease is commonly called lobar pneumonia, involvement of a whole lobe or nearly a whole lobe is not an essential character of alveolar pneumonia in children. In our experience, it is more usual to find consolidation of a part of a lobe or lobes. There is far more variation in the extent of consolidation in the alveolar pneumonia of childhood than in the corresponding disease (lobar pneumonia) of adult life. While it may be very extensive, the pneumonic area is often relatively smaller in children than is usual in adults. If this be true of fatal cases, it is likely to be even more often true of the slighter cases which recover : and this is confirmed by clinical experience. At the same time, it should be pointed out that a majority of our cases showed pneumonia in more than one lobe : but it does not follow, of course, that this is of equally frequent occurrence in non-fatal cases. It is apparently rather unusual for an entire lung to be completely consolidated.

Appearance of the pneumonic area.—When pneumonia in a child is encountered at autopsy, the problem which confronts the pathologist is the diagnosis between alveolar pneumonia and confluent broncho-pneumonia. In typical cases the question is not a difficult one, for an area of alveolar pneumonia presents certain well-defined macroscopic characters by which it may be distinguished from confluent broncho-pneumonia.

The affected part, no matter of what extent, is massively and completely consolidated. As every alveolus is filled with exudate, no collapse is present within the area, which accordingly projects well above the level of neighbouring unconsolidated lung. Its consistence is solid, firm, and uniform. It lacks the nodular character and somewhat rubber-like resilience which in most broncho-pneumonic lungs, even of the most confluent type, are produced by an alternation of zones of complete consolidation with zones of partial collapse within the affected part. Where the pneumonic area abuts upon aerated lung substance, the margin is usually extremely definite (Plate II, Figs. 6 and 7). This also is a point of difference between alveolar pneumonia and confluent broncho-pneumonia.

Should the pneumonia extend to the surface of the lung, the pleura overlying it is invariably inflamed. Usually there is only a thin layer of dry fibrinous exudate, and this may or may not be present beyond the limits of the pneumonic area. Apart from the cases in which empyema had developed, we have rarely seen either a copious fibrinous exudate or a pleurisy with effusion. It is probably true to say that in childhood cases, in which the pleurisy is severe, usually go on to empyema.

On section, the appearance of the pneumonic area naturally depends upon the stage which has been reached. If resolution has not begun, the cut

surface has a dry, dull appearance and the projection of plugs of exudate from the alveoli often imparts to it a finely granular character. This differs from the appearance of a broncho-pneumonic lung, which on section usually presents a moist and shiny surface.

The colour varies from red to grey according to the stage of the disease. Most of our cases were at the stage of early grey hepatization at the time of death, but there were several examples of red hepatization. The colour of the cut surface is usually fairly uniform, but rarely perfectly so. Alternations of red and grey are often present throughout the patch due to differences in the composition of the exudate ; but these variations in colour are independent of the distribution of bronchi, and the appearance of mottling produced by them is quite different from the definite peri-bronchial mottling which is characteristic of broncho-pneumonia. In early cases there is often a zone of intense hæmorrhagic congestion at the spreading edge of the patch.

Bronchi and bronchioles within the pneumonic area are not conspicuous ; do not show inflammatory thickening of their walls ; are not noticeably dilated ; and do not contain large quantities of pus, although a certain amount of exudate is present in them. In unconsolidated parts of the lungs the bronchi are healthy. The absence of bronchitis, especially of the smaller tubes, in those parts where there is no consolidation is an important feature of typical alveolar pneumonia. Some hyperæmia of the mucous membrane of the large bronchi and of the trachea, and the presence therein of exudate derived from the pneumonic area, are usual.

Apart from the definite patch or patches of pneumonia, the lungs are free from consolidation. There is usually some general congestion, and a degree of acute vesicular emphysema may be present, but usually very much less than in broncho-pneumonia. Interstitial emphysema, which is of common occurrence in broncho-pneumonia, we have never seen in a case of alveolar pneumonia.

The tracheo-bronchial and root glands show swelling and active hyperæmia (Plate I, Fig. 3), but the very great enlargement and intense inflammation of these glands, so often associated with broncho-pneumonia (Plate II, Fig. 8), have not been found in any case in our series.

Morbid Histology.

In the pneumonic area complete consolidation of the whole part affected is a constant feature. Every alveolus is filled with exudate, and areas of collapsed or partially collapsed alveoli are not present.

The exudate.—There is considerable variation in different cases in the composition of the exudate which fills the alveoli, depending partly, but not entirely, upon the stage of the disease. There would seem to be a tendency for the exudate to be of a more cellular and relatively less fibrinous character in children than in adults. This is true especially in very young children, in whom departure from the typical standard of the adult case is apt to be greater in this and in other respects. Nevertheless, this rule is not of universal

application, for even in infants the exudate may be composed mostly of fibrin. Fig. 9 (Plate III), which is taken from the lung of a male infant, aged 9 months. shows an exudate in which fibrin greatly preponderates.

There is always some variation in the composition of the exudate in different parts of the pneumonic area ; and, as in adult cases also, the more cellular parts are often those nearest to the terminal bronchiole, the outlying alveoli of the lobule containing a more fibrinous exudate. In certain cases, which in other respects conform to the alveolar type, there is very little formation of fibrin, and the exudate is almost entirely composed of polymorphonuclear leucocytes. We are of opinion that the amount of fibrin in the exudate is not a reliable guide in differentiating alveolar pneumonia from broncho-pneumonia, especially when only small sections are used, and the microscopic examination is thus confined to a limited portion of the consolidated part. Most lungs with confluent broncho-pneumonia contain areas in which fibrin is as plentiful in the alveoli as in any case of croupous pneumonia in child or adult.

The alveolar walls.—It is characteristic of alveolar pneumonia that the products of inflammation are thrown out into the alveolar spaces and that the walls do not show any marked degree of infiltration with inflammatory cells (Plate III, Fig. 10). Congestion of capillaries in the early stages, and sometimes swelling of the lining epithelium before it is cast off, may cause the walls to look somewhat thicker than in health (Plate III, Fig. 9) ; but the dense infiltration with inflammatory cells, which so greatly obscures the alveolar walls in broncho-pneumonia, is characteristically absent in the alveolar type.

The bronchi.—Within the pneumonic area the bronchi always contain inflammatory exudate which resembles that present in the alveoli, although it is often relatively richer in leucocytes. When the alveolar exudate is fibrinous, the bronchi are often plugged with fibrino-cellular exudate, a condition rarely seen in broncho-pneumonia. When the exudate in the alveoli is of a very cellular type, in the bronchi it may have an almost purulent character. Evidence of severe inflammation of the bronchi themselves is, however, absent in typical cases. If it be present, the case is either atypical, or the diagnosis of alveolar pneumonia is mistaken. The blood vessels of the bronchial wall may share to some extent in the general hyperæmia of the part ; but the wall is not significantly swollen, nor infiltrated with polymorphonuclear cells, and quite often even the epithelial lining remains surprisingly intact (Plate III, Fig. 11). The healthy condition of small bronchi in the midst of an area of consolidation is clearly shown in Fig. 12 (Plate III).

In some of our cases, especially those of young children, a certain amount of lymphocytic infiltration has been found in the bronchial walls in the pneumonic area. Some observers hold that this is characteristic of broncho-pneumonia, and would classify as such any case in which it was found. Our experience has been that in broncho-pneumonia the cellular infiltration of the bronchial walls is much more severe ; that among the infiltrating cells polymorphonuclear leucocytes rather than lymphocytes predominate ; that the walls are greatly swollen in addition to being infiltrated ; and that the lining epithelium is usually destroyed. In the absence of other evidence of acute

inflammation of the bronchial wall, a certain amount of lymphocyte infiltration need not be regarded as inconsistent with a diagnosis of alveolar pneumonia. The lymphocytes are probably derived from the microscopic lymph nodes which occur normally in the walls of bronchi and readily undergo hyperplasia in the presence of any inflammation in their neighbourhood.

Interlobular septa and perivascular stroma.—There are often large deposits of fibrin in the interlobular septa, causing them to be greatly broadened out so that they form a conspicuous feature of the section (Plate III, Fig. 13). A certain number of polymorphonuclear leucocytes may be entangled in the fibrin meshwork. Dense aggregations of leucocytes in the septa are unusual. We have found this fibrin deposit in the septa very frequently in cases of alveolar pneumonia, and comparatively seldom in broncho-pneumonia, even where there has been extensive confluence. The perivascular fibrous tissue may show the same condition, but often it is remarkably free from any inflammatory change (Plate III, Fig. 12). Sub-pleural and septal lymphatic vessels may be dilated and filled with a fibrinous coagulum. The pleura practically always shows an exudate, usually scanty and mostly fibrinous except when empyema is present.

The margin of the pneumonic area. When the area of pneumonia abuts upon unconsolidated lung, the edge is a fairly definite one (Plate II, Fig. 6). Sometimes the consolidated patch is bounded in part by interlobular septa, but a boundary of that kind is rarely complete along the whole extent of the patch. If the pneumonia be still spreading at the time of death, there may be a narrow zone of intense congestion and hæmorrhage at the edge of the consolidated area. Sometimes there is merely a zone in which the capillaries in the alveolar walls are congested and the spaces contain an œdematous material. In either case the appearances at the spreading edge suggest an extension of the inflammation by continuity from alveolus to alveolus in a more or less uniform manner all along the margin of the patch. This is quite different from the manner of spread in broncho-pneumonia, which is by way of the bronchi, so that beyond the edge of an area of confluent broncho-pneumonia outcrops of consolidation appear in small patches surrounding bronchioles (Plate II, Fig. 8).

In unconsolidated parts of the lungs the alveoli and bronchi alike are free from inflammatory exudate. Apart from some general hyperæmia and perhaps slight acute vesicular emphysema, the parts of the lungs which are not consolidated are healthy. This is exceedingly characteristic of typical alveolar pneumonia (Plate I, Figs. 2 and 4, and Plate II, Fig. 6), and is in sharp contrast to the state of affairs in confluent broncho-pneumonia (Plate II, Fig. 8).

Discussion.

The features of alveolar pneumonia to which special importance is attached in distinguishing it from confluent broncho-pneumonia are the following :— the localization of consolidation to a certain definite area ; the absence of generalized bronchitis ; the absence of anything more than a very trivial

inflammation of the bronchi within the pneumonic area ; the freedom of the bronchial and alveolar walls and stroma generally from damage by infiltration with inflammatory cells.

The last of these deserves special emphasis. Alveolar pneumonia, in marked contrast to broncho-pneumonia, is a disease in which the inflammatory reaction results in the throwing out of the products of inflammation upon the surface (*i.e.*, the alveolar spaces), and in which the substance of the lung shows no severe or persistent involvement. A reason for this immunity of the interstitial frame work may be found in the fact that the infection is located in the alveoli, whose walls possess no lymphatics. Invasion of the lymphatics of the lungs by the infection, with consequent lymphangitis and acute interstitial inflammation, is therefore not liable to occur. In broncho-pneumonia, on the contrary, where the infection is centred chiefly in the bronchi whose walls possess a rich network of lymphatic vessels which are readily invaded, the occurrence of lymphangitis and acute interstitial inflammation is obviously a strong probability.

According to Blake and Cecil[9], however, lobar pneumonia experimentally produced in monkeys begins as a lymphangitis in the walls of bronchi which is followed by alveolar inflammation ; and with the onset of consolidation of the alveoli, this lymphangitis passes off. The application of this result to human cases has yet to be demonstrated, but if it be correct, it is significant that the lymphangitis is not persistent or progressive, but a transient affair which disappears when the inflammatory reaction is fully established and the infection passes out into the alveolar spaces.

The absence of persistent lymphangitis and inflammatory involvement of the interstitial framework of the lungs in alveolar pneumonia is a significant pathological feature which has an important bearing upon certain clinical features of the disease. The relatively short course, the abrupt termination of serious symptoms, and the rapid return of the lung to a normal state, which are characteristic of alveolar pneumonia in cases which recover, would all be unlikely, if not impossible, in the presence of severe interstitial inflammation and lymphangitis. Further, because the alveolar septa and bronchial walls suffer no disorganization during the active stage of the inflammation, when recovery occurs the exudate is removed from the alveoli by resolution and there is no occasion for a process of reorganization. Therefore, the lung is able to recover perfectly and rapidly, without permanent change in structure which would inevitably cause disablement of function. Hence the comparative rarity of such conditions as fibrosis or bronchiectasis occurring as a sequel of alveolar pneumonia.

Atypical cases. It is clear that in typical cases it is no very difficult matter to distinguish between alveolar pneumonia and confluent broncho-pneumonia, for there are many points of difference sufficiently clearly defined. But from time to time cases are met with which are really difficult to place in either category, because of their atypical features. Among the cases which present this problem there are two groups :—(*a*) those which deviate in some important particular from the picture of alveolar pneumonia which has been

described: (*b*) those in which one part of the lung presents the typical picture of alveolar pneumonia, while obvious broncho-pneumonia is present in other parts.

For the purpose of classification in our series, all cases of the latter kind were excluded from the alveolar pneumonia group. With regard to the former, every case must be considered on its merits. In our series, a few cases which presented certain atypical features were classified as alveolar pneumonia, because, after due consideration, the weight of evidence was held to be in favour of that diagnosis. Atypical cases are most frequent in the earlier age periods. After the age of two years the cases tend more and more to approximate to the adult type of 'lobar' pneumonia.

The most important deviation is the involvement of the bronchi within the pneumonic area in active inflammation. No case in which this occurs can be regarded as typical alveolar pneumonia. But we have occasionally found it in cases which in other respects conformed strictly to the alveolar type. The bronchi may be denuded of epithelium, their walls invaded by inflammatory cells and much swollen: in one of our cases they had even suffered considerable disorganization and showed a degree of acute dilatation (Plate II, Fig. 5).

Some observers would undoubtedly class such a case as broncho-pneumonia. Yet, if in all other respects the pathological picture be typically that of alveolar pneumonia, it would appear to us to be more correctly placed in that group. Our experience has led us to believe that the inflammation of the bronchial walls in cases of this kind is probably secondary to a primary alveolar pneumonia, and is not the primary manifestation of infection as in broncho-pneumonia. In other words, it is possible that occasionally the infection, instead of remaining localized in the alveolar spaces, may spread to the bronchi and invade their walls as a secondary development. This is a serious occurrence which, it may be supposed, increases the gravity of the disease and prejudices the chances of recovery. It may be that it seldom, if ever, occurs in cases which recover: even in fatal cases it is rare.

Obviously in cases of this kind the pathological diagnosis must remain in doubt, and a matter of personal opinion. In the Glasgow series[8], all such cases were evidently classed as broncho-pneumonia. We have retained some of them in our alveolar pneumonia group. We would venture to express the opinion that in some of these doubtful cases it would be impossible to come to a reliable decision by a study of the limited field available in ordinary small microscopic sections, and in this respect the whole-lung sections which we have been able to use are of great importance.

Illustrative Cases.

Case 1. *Double pneumonia of alveolar (lobar) type.* (Plate I, Figs. 1 and 2). Female, aged 3 years, seventh child. Mongolian imbecile. Breast-fed for 18 months. History of diphtheria, with good recovery, seven weeks before the fatal illness. Fat, flabby child. Died within 24 hours of admission after an illness of sudden onset and of six days' duration. Physical signs of consolidation in both lungs. Large heart and marked evidence of circulatory failure.

On post-mortem examination, the right upper lobe was partially and the left lower lobe more completely consolidated. The pneumonic areas were of a deep red colour and the overlying pleura was inflamed. The remaining lobes were free of pneumonia and showed some

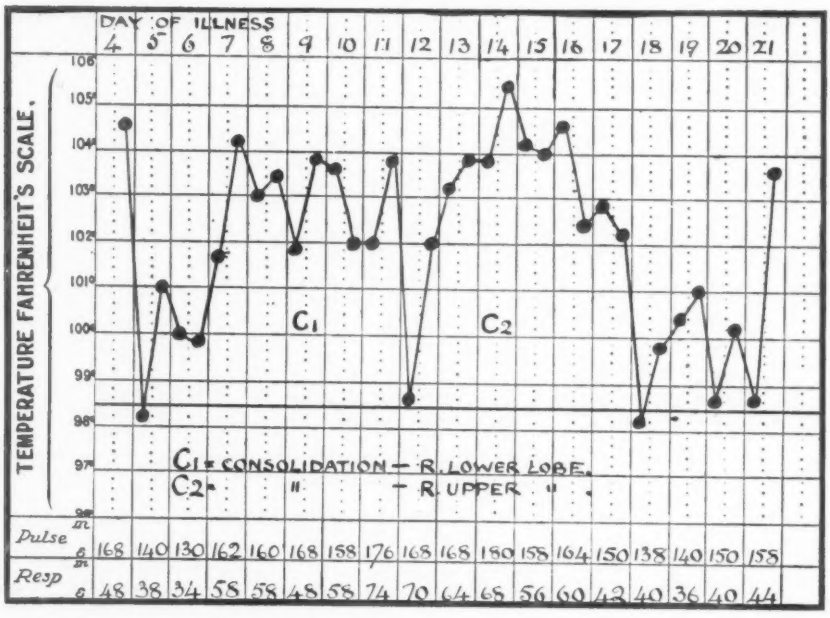
emphysema. No general bronchitis was present. There was marked enlargement of the heart, especially on the right side, in association with a large defect in the membranous part of the septum.

Microscopically, the pneumonia in both lungs was at much the same stage (red hepatization). There was no doubt as to its alveolar character. There was the usual exudate in ,and trivial inflammation of, the bronchi in the consolidated lobes. Both lungs showed evidence of previous damage —a slight fibrosis of unequal distribution, arterial changes, and lymphocytic accumulations in bronchial and other connective tissues. There was no history of a former illness, but this finding was not surprising in view of the susceptibility of mongols to respiratory infections.

Case 2. *Pneumonia of alveolar type, with relapse.* (Plate I, Figs. 3 and 4). Male, aged 10 months. Second child of unemployed father; home conditions bad. Breast-fed. No previous illnesses. General condition good. Five teeth. Died after a three weeks' illness, in which there were three distinct pyrexial periods in close proximity, followed by low fever in the last few days (Chart I).

CHART I.

Relapsing Alveolar Pneumonia (Case 2).



The child was not under observation during the first period. The second was associated with consolidation of the right lower, and the third with consolidation of the right upper lobe. During the latter there were signs of meningeal irritation. The left lung remained unaffected throughout.

Post mortem, the left lung and right middle lobe were healthy. The right lower lobe was the seat of an almost completely resolved pneumonia, with early organization of the overlying pleural exudate. The right upper lobe, with the exception of the apex and anterior border, was consolidated; the pneumonia recent; the colour and consistence fairly uniform; the margin sharp; the pleura acutely inflamed. The bronchi contained some pus. There was little to note elsewhere in the body.

On microscopic examination, the left lung showed merely superficial catarrh of the larger air-passages. In the right lower lobe, remnants of exudate in alveoli and the presence of large mononuclear cells provided ample evidence of a recent pneumonia in the final stages of resolution. The process was least advanced in the portion of the lobe adjacent to the root. There was catarrhal desquamation of the epithelium of bronchi, but no active inflammation. In the

PLATE I.

Figs. 1 and 2.—Double alveolar pneumonia in girl of 3 years (illustrative Case 1). Consolidation of right upper and left lower lobes.

Figs. 3 and 4.—Alveolar pneumonia in boy of 10 months (illustrative Case 2). Pneumonia resolving in right lower lobe. More recent consolidation of most of right upper lobe. Left lung unaffected. A = Lymphatic gland at root of right lung.

PLATE II.

Fig. 5.—Alveolar pneumonia in boy of 5 months (illustrative Case 3). Almost complete consolidation of right lung. Some dilatation of bronchi.

Fig. 6.—Alveolar pneumonia in boy of 14 months. Consolidation of half of left lower lobe.

Fig. 7.—Alveolar pneumonia in boy of 4 months. Consolidation of small area at base of right lung.

Fig. 8.—Confluent broncho-pneumonia in boy of 1 year, included for purposes of contrast with preceding illustrations of alveolar pneumonia.

PLATE III.

Fig. 9.—×120. Alveolar pneumonia in boy of 9 months showing uniform fibrino-cellular exudate in alveoli, with thickening of alveolar walls due to congestion of capillaries and swelling of endothelial and alveolar lining cells.

Fig. 10.—×300. Alveolar pneumonia in boy of 4 years and 9 months, showing fibrino-cellular exudate in alveoli. Rather later stage than above. No swelling or infiltration of alveolar walls.

Fig. 11.—×150. Alveolar pneumonia in girl of 3 years (same case as Figs. 1 and 2). Bronchus in pneumonic lobe, showing relative freedom from inflammation and intact epithelium.

Fig. 12.—×100. Alveolar pneumonia in boy of 9 months (same case as Fig. 9). Small bronchi (B) in consolidated area, with exudate in lumina but undamaged walls. Perivascular connective tissue also free from infiltration. A = Blood-vessels.

Fig. 13.—×120. Alveolar pneumonia in boy of 9 months (same case as Figs. 9 and 12). Interlobular septum broadened as result of deposit of fibrin.

PLATE I.

Fig. 1.

Fig. 2.

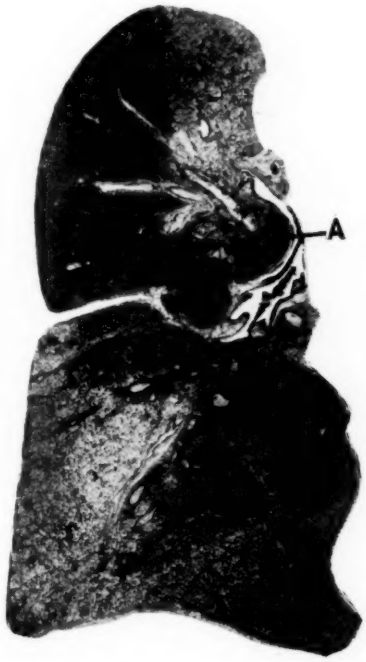


Fig. 3.

Fig. 4.

PLATE II.

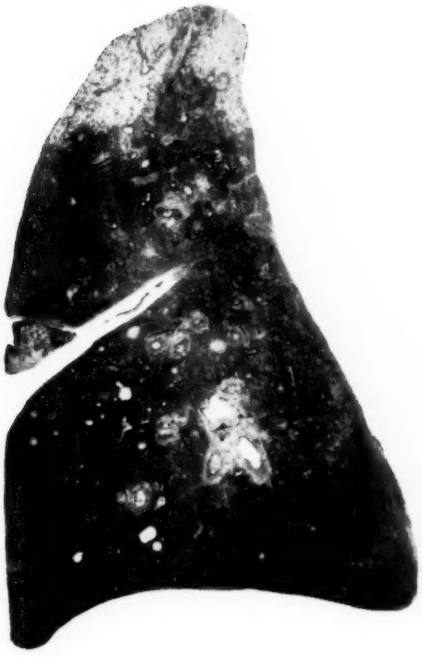


Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

PLATE III.

Fig. 9.

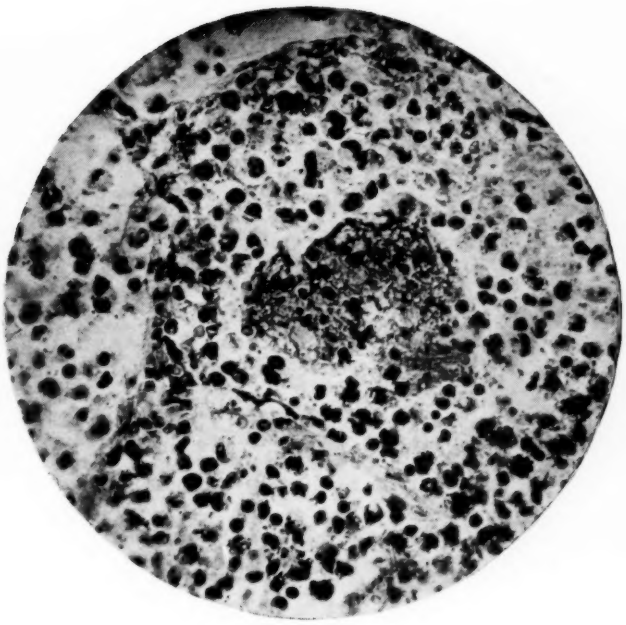


Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13.

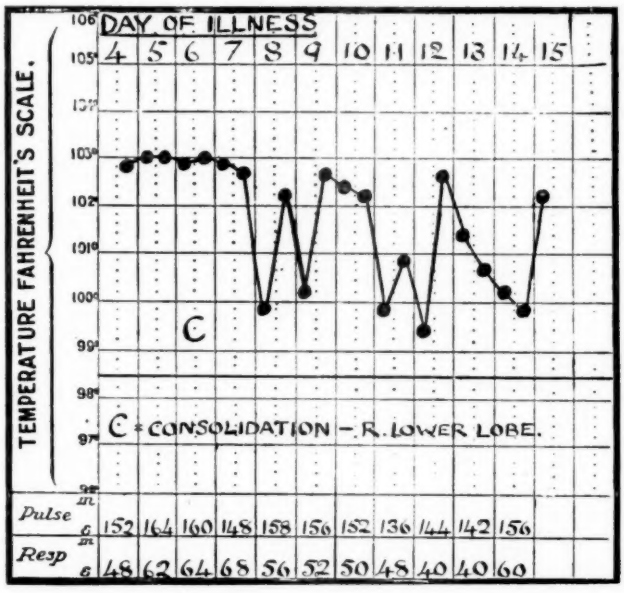
right upper lobe, the pneumonia was of alveolar type. Alveoli were completely filled with fibrinous exudate containing polymorphonuclear and catarrhal cells; alveolar walls clearly distinguishable and not infiltrated with inflammatory cells; the exudate was of the same type throughout and not 'zonal' in distribution as in broncho-pneumonia. The bronchi showed up clearly owing to the presence of a cellular exudate, but the epithelium was intact and the substance of the walls not appreciably inflamed. The interlobular septa were œdematous. There was recent exudate on the pleural surface.

The diagnosis of alveolar pneumonia was clear on clinical and pathological grounds.

Case 3. *Alveolar pneumonia involving most of one lung, with a patch in the lower lobe of the other lung.* (Plate II, Fig. 5.) Male, aged 5 months. Third child. Mother died of puerperal septicæmia. Fed on cow's milk mixtures. Fatal illness lasted two weeks (see Chart II.). Onset

CHART II.

Alveolar Pneumonia (Case 3).



of acute symptoms sudden but preceded by 'cold in head.' Pale (rather thin) infant, with signs of early rickets. Consolidation noted in right lower lobe on sixth day; spread to involve most of lung posteriorly. Effusion suspected but not confirmed by exploration. Cough short and obviously painful. Breathing rapid but not embarrassed. Some accompaniments in left lung throughout illness, but no pneumonia detected.

On post-mortem examination, the whole right lung, except for the middle lobe and the apical portion of the upper lobe, was solid. The colour was a more or less uniform greyish-red. There was well-marked bronchitis, but an absence of peri-bronchial mottling. A thick fibrinous deposit was present on the visceral pleura. The left lung contained an irregularly shaped but fairly well-defined patch of pneumonia in the substance of the lower lobe. It showed no other area of consolidation. The appearance of the pneumonic patch was not that of confluent broncho-pneumonia.

Microscopic examination confirmed the presence of rather severe bronchitis in the consolidated parts; some of the bronchi, in the right lung especially, were denuded of epithelium and appreciably dilated. Nevertheless, the pneumonia in its uniformity and other characters was essentially alveolar in type, not only in the extensively involved right lung but also in the partially consolidated left lower lobe, and no doubt was felt in so diagnosing the case,

SUMMARY.

1. An analysis of twenty-three autopsies in cases of alveolar (lobar) pneumonia in young children is given. Eighteen were under two years of age.

2. The study of this post-mortem material supports the view widely held on clinical grounds that this type of pneumonia is not uncommon in the first two years of life.

3. The morbid anatomy and histology of alveolar pneumonia in infancy and early childhood are described.

4. Atypical forms of alveolar pneumonia in children are briefly discussed.

5. Short clinical and post-mortem reports of three cases of alveolar pneumonia, two of them in infants under one year, are presented.

6. In this study, paraffin sections of entire lungs have been used. Illustrations of these are given.

The large sections illustrated in this and the succeeding papers are the work of Mr. T. D. Hamilton of the Royal College of Physicians' Laboratory, Edinburgh.

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THE ESTIMATION OF THE PHASE OF THE DISEASE IN RICKETS.

BY

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In many diseases, particularly in those with a tendency to spontaneous cure, various therapeutic agents have been unjustifiably credited with possessing valuable curative properties. In perhaps no instance is this more striking than in the case of rickets, in which claims have been made for the efficacy of many different forms of treatment.

Much of the misunderstanding in the question in the case of rickets has arisen from the want of certainty in the examples tested whether the disease was in a progressive or a retrogressive stage. At the outset therefore of any investigation it is essential that we have standards by which this matter may be decided, and the present communication deals with this aspect of the problem, namely, the relative value of different methods of determining the phase of the disease.

It has frequently been the custom to decide whether an individual example ot rickets were active or healing from an isolated radiological examination. We have not infrequently noted, however, that a case of rickets which has been judged from a single radiological examination to be active may, within 2 to 3 weeks, and that in spite of the conditions remaining the same, show unequivocal radiographic evidence of healing. Experience has taught us that it may also take this time after the inception of healing, or at least after the administration of efficient cod-liver oil, before definite signs of healing are visible radiologically. It has been our custom, therefore, in order to establish the activity of the disease, to require radiograms failing to reveal any evidence of healing taken at an interval of three weeks. But as this method involves the expenditure of a considerable amount of time, a pre-observation period of at least three weeks, it was hoped that a study of the behaviour of the inorganic phosphorus content of the blood serum, and the retentions and modes of excretion of calcium and phosphorus, might provide data on which to base a simple and time-saving, but still reliable, test of the stage of the disease.

The findings from this point of view are considered under two headings, namely, (1) that dealing with the inorganic phosphorus content of the serum, and (2) that dealing with the metabolism of calcium and phosphorus.

1. The Inorganic Phosphorus Content of the Blood Serum.

Many observations have been made on the variations of the inorganic phosphorus content of the blood serum in rickets. Iverson and Lenstrup[1] in 1920 published the results of a study of the concentration of acid-soluble, acid-insoluble, and total phosphorus of the plasma and whole blood of normal

and rachitic infants. They found that in rickets the acid-soluble phosphorus was low. A year later Howland and Kramer[2] described a definite lowering of the inorganic phosphorus of the serum in active rickets. They based their diagnosis of the stage of the disease on clinical grounds supported by radiograms. In 16 non-rachitic children the inorganic phosphorus varied from 4 to 7·1 mgrm. per 100 c.cm. of serum. In 22 rachitic children it varied from 0·6 to 3·2 mgrm. per 100 c.cm. of serum. From a study of the calcium and inorganic phosphorus of the serum in children with uncomplicated rickets, and with rickets complicated by tetany, Howland and Kramer were led to believe that the determining factor in the calcification of the bones is the presence of calcium and phosphorus in such amounts that the product of their concentration in mgrm. per 100 c.cm. of serum equals a certain minimal figure, which ranges between 30 and 40. In rickets they found that the concentration of calcium in the majority of instances is essentially normal, whereas the phosphorus concentration is definitely low.

Hess and Unger[3], however, state that a low inorganic phosphorus does not indicate whether the rachitic process is healing or advancing, since they have met with examples where radiological examination revealed healing although the inorganic phosphorus had increased but little from the previous low figure found during the active phase. These authors considered that the most valuable criterion of healing was the radiogram. A year later Hess, Calvin, Wang and Felcher[4] concluded that consecutive blood examinations are of greater importance than radiographic evidence in the determination of the stage of rickets.

In the present investigation the behaviour of the inorganic phosphorus of the serum was studied in order to determine the relative value of (1) a single observation, and (2) a series of observations. The observations were controlled by X-ray findings. Tisdall's[5] method was employed for the estimations of the inorganic phosphorus of the serum, and in most of the cases the calcium concentration of the serum was also determined, the method used being that of Kramer and Tisdall[6].

Single observations were made in 27 cases which have been classified into 3 groups according to the radiological appearances :—

Group I includes 7 cases of rickets in which radiograms taken at weekly intervals over a period of 3 weeks showed no evidence of healing.

In Group II are included 8 cases in which the observations were made at the time when the first appearance of healing radiographically declared itself.

In Group III are 12 cases in which radiographic evidence of healing had been in progress for at least 2 weeks. In all of these cases the serum calcium was normal.

In Group I (active rickets) the inorganic phosphorus of the serum varied between 2·1 and 3·8 mgrm. per cent. with an average of 2·9 mgrm. In Group II (early healing) the serum phosphorus varied between 2·5 and 5·8 mgrm. per cent., the average value being 3·9, and in Group III (more advanced healing) the serum phosphorus was still definitely higher, varying between 3·8 and 6·5 mgrm. per cent., with an average of 5 mgrm. (Table I).

TABLE I.

SINGLE OBSERVATIONS ON SERUM PHOSPHORUS IN RICKETS.

Stage of disease.	No. of cases.	Inorganic Phosphorus of Serum.		
		Maximum value. mgrm. %	Minimum value. mgrm. %	Average value. mgrm. %
Active (Group I.)	7	3·8	2·1	2·9
Early healing (Group II.)	8	5·8	2·5	3·9
More advanced healing (Group III.)	12	6·5	3·8	5·0

Table II shows the products of the calcium and inorganic phosphorus contents of the serum in the three groups of cases.

In Group I this product varied between 22 and 36, the average being 28 ; in Group II it varied between 24 and 60, with an average of 38 ; and in Group III between 38 and 68, with an average of 52.

TABLE II.

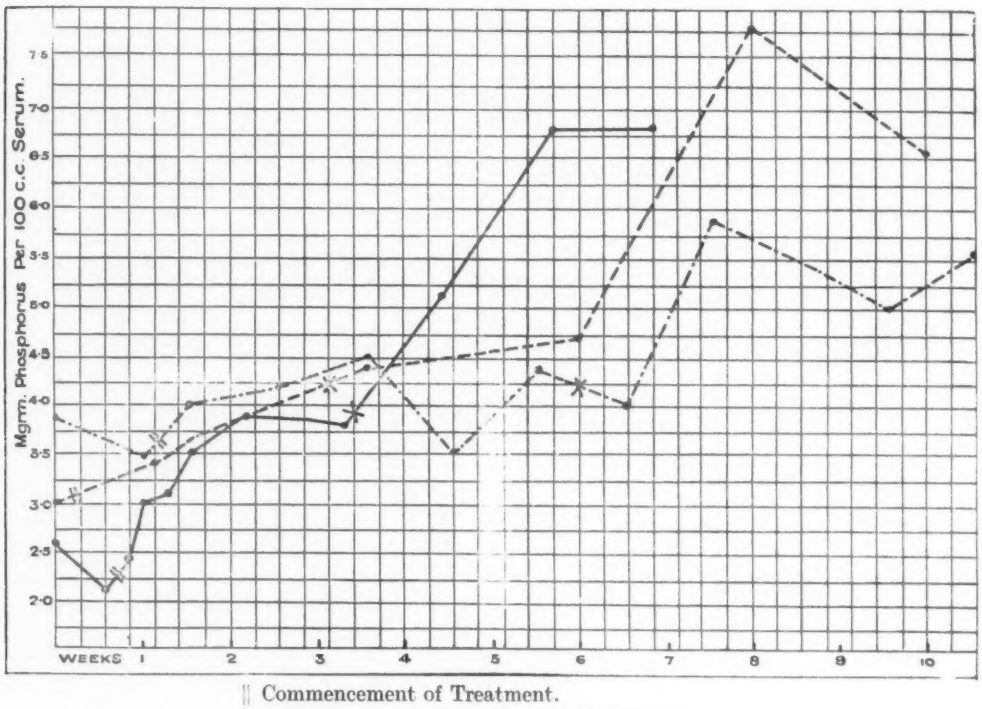
PRODUCTS OF THE CALCIUM AND INORGANIC PHOSPHORUS CONTENTS OF THE SERUM IN RICKETS.

Stage of disease.	No. of cases.	Product of Calcium and Phosphorus of Serum.		
		Maximum.	Minimum.	Average.
Active (Group I.)	7	36	22	28
Early healing (Group II.) ...	6	60	24	38
More advanced healing (Group III.)	11	68	38	52

In each of six cases of rickets a series of observations on the serum phosphorus was obtained during the active and healing phases. In one patient in this group healing commenced spontaneously, but in each of the other five healing was induced by one or other of the recognized forms of treatment. In the treated cases (Charts I and II) the general level of the serum phosphorus rose before radiological examination revealed healing. Subsequent, however, to the appearance of healing in the radiographic picture, the serum phosphorus showed a further and more marked increase. In the case of spontaneously healing rickets (Chart III), the inorganic phosphorus of the serum fell from 3·4 to 2·5 mgrm. per cent. over a period of two weeks, during which time progressive healing was apparent in the successive X-ray pictures.

CHART I.

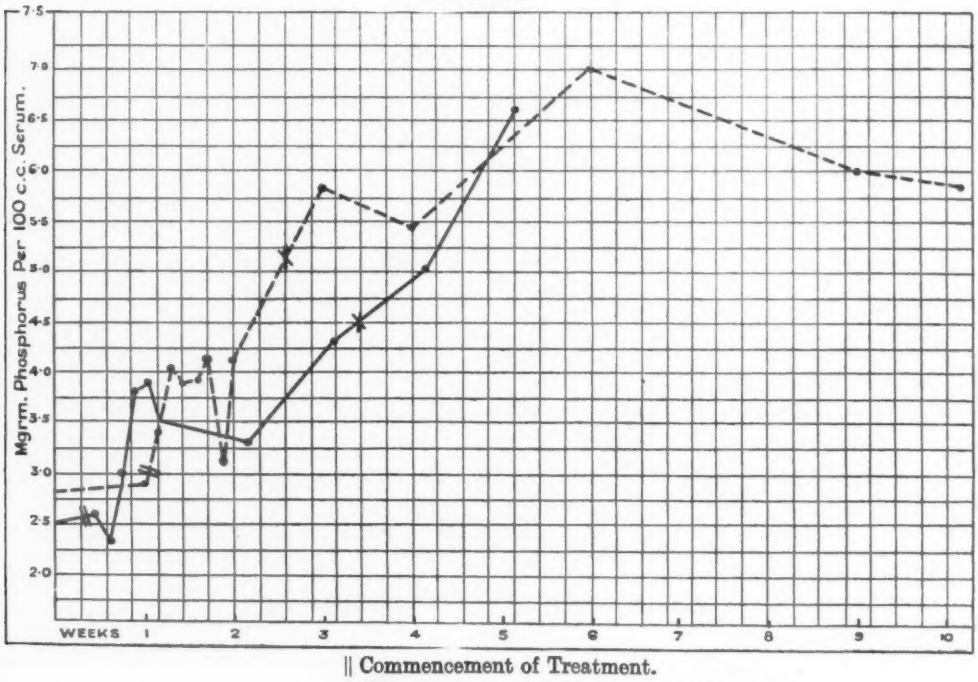
INORGANIC PHOSPHORUS CONTENT OF SERUM IN THREE CASES OF RICKETS BEFORE AND DURING TREATMENT.



‖ Commencement of Treatment.
× First appearance of Healing in Radiograms.

CHART II.

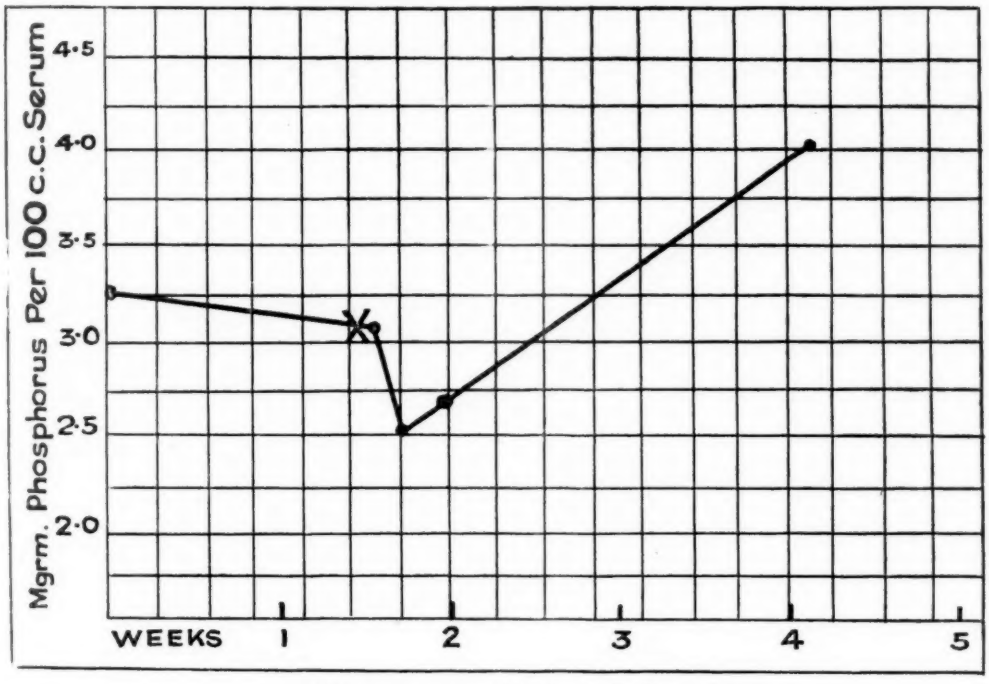
INORGANIC PHOSPHORUS CONTENT OF SERUM IN TWO CASES OF RICKETS BEFORE AND DURING TREATMENT.



‖ Commencement of Treatment.
× First appearance of Healing in Radiograms.

CHART III.

INORGANIC PHOSPHORUS CONTENT OF SERUM IN CASE 3 WITH SPONTANEOUS HEALING.



First appearance of Healing in Radiograms.

Discussion.

(1) *Isolated observations.*—A study of the results of the isolated determinations of the serum phosphorus shows quite clearly that the average values in active, slightly healing, and more advanced healing rickets are in ascending order. It is, however, equally noteworthy that there is a very marked overlapping of the figures of these groups, the value 3·8 mgrm. per cent. being common to all three. One must therefore conclude that an isolated observation of the serum phosphorus cannot be taken as an unequivocal index of the stage of the disease.

(2) *Product of the calcium and phosphorus contents of the serum.*—It will be noted that in all the cases of active rickets the product of the calcium and inorganic phosphorus contents of the blood serum is below the upper limit of 40 described by Howland and Kramer for active rickets. That this limit, however, is of no practical value for determining the activity of the disease is shown by the fact that three (50 per cent.) of the cases of early healing and one (9 per cent.) of these presenting more advanced healing also showed products below this limit.

(3) *Serial observations.*—As can be seen from Charts I, II, and III the serum phosphorus rises as healing progresses in all cases except Case 3 (see Chart III). In this last patient early healing, as indicated by radiograms, is accompanied by a slight fall in the serum phosphorus value, but it should be

noted that this is the only case in which a series of observations was obtained during spontaneous healing and from it, therefore, far-reaching conclusions cannot be drawn.

In the other patients, in all of whom healing followed some definite course of treatment, the value for the serum phosphorus showed a considerable increase before the appearance of X-ray evidence of healing. This increase exceeded in three cases the maximum value obtained in admittedly active rickets, and in the other two cases reached the upper limit of the values obtained in the active group. The question arises as to the significance of this rise, and it might be suggested that it should be taken as evidence of healing occurring previous to the appearance of a positive X-ray finding. In support of this view is the fact that on the whole the rise in serum phosphorus, once commenced, is fairly steady. There are, however, occasional falls but the main tendency as shown in the graphs is upward. It would naturally be expected that such a rise would occur before increased calcification of the bones could be detected radiographically, and it is probable that a steady rise in the value for serum phosphorus is evidence of healing despite the absence of positive X-ray findings.

2. The Metabolism of Calcium and Phosphorus.

That there is a diminution in the retention of lime in active rickets is well recognized. Schabad[7] in 1911 found a very low calcium retention in early rickets, in fact in some instances more lime was excreted than was ingested. In cases of longer duration he found that the retention returns to normal, or is increased above the normal, before any clinical signs of recovery are apparent. With the lowering of the retention of lime there occurs a corresponding decrease in the retention of phosphoric acid due to an increased elimination of P_2O_5 in the fæces. Some years later Findlay, Paton and Sharpe[8] in studies of the calcium metabolism in rickets found an increased excretion of lime during the active stage, but in no instance did they obtain a negative balance, *i.e.*, more excreted than ingested. These authors pointed out for the first time that the metabolic picture differs according to the activity or non-activity of the disease and not according to its duration. Five years later Telfer[9], confirming their findings, drew attention to the difference in the mode of excretion of P_2O_5 in the active and healing phases. He showed that during the active period the greater part of the phosphorus is excreted in the fæces, and during the healing stage the urine contains the larger amount. Thus in active rickets the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ is less than unity, and during healing it is much greater than unity.

The metabolism studies forming the basis of the present communication were made in cases of active rickets, in cases of spontaneously healing rickets and in examples of rickets where healing had been induced by treatment. The three groups comprise in all five cases. Two observations were obtained in patients during the active stage of the disease, three observations during a spontaneously healing phase, and two observations during a period of healing induced by treatment.

The diet given was undiluted cow's milk and each child was kept on this diet for three days before the metabolic study was commenced. The urine and fæces were collected for seven days. The analyses of P_2O_5 in the milk, urine and fæces, and the analyses of lime in the urine, were made by the usual gravimetric methods. The CaO in the milk and fæces was precipitated as oxalate, the precipitate washed and titrated with $\frac{N}{10}$ $KMnO_4$.

The results are given in Table III.

TABLE III.

METABOLISM OF CALCIUM AND PHOSPHORUS IN ACTIVE RICKETS, TREATED RICKETS, AND SPONTANEOUSLY HEALING RICKETS.

Case No.	X-ray findings before metabolism study.	X-ray findings after metabolism study.	Treatment.	CaO in urine. Percentage total output.	Ratio of P_2O_5 in urine to P_2O_5 in fæces	Daily retention per kgrm. body weight.	
						CaO grm.	P_2O_5 grm.
1. D.D.	active	active	nil.	0·3%	$\frac{1}{2·7}$	0·04	0·04
2. D.B.	active	active	nil.	0·4%	$\frac{1}{1·6}$	0·04	0·04
1. D.D.	active	healing	Irradiation	3·7%	$\frac{4·7}{1}$	0·25	0·22
2. D.B.	active	healing	Radiostol	2·6%	$\frac{4·4}{1}$	0·10	0·08
3. J.P.	active	slight healing	nil.	0·4%	$\frac{2}{1}$	0·07	0·07
4. H.W.	? healing	definite healing	nil.	0·8%	$\frac{1}{3·1}$	0·05	0·08
5. D.B.	healing	further healing	nil.	1·9%	$\frac{2·4}{1}$	0·13	0·13

The following is a brief description of the cases.

CASE 1. D. D., æt. $2\frac{1}{2}$ years, was kept under observation for three weeks during which period radiographic examination showed no evidence of healing. A metabolism study was then made. The daily retentions of CaO and P_2O_5 were each ·04 grm. per kgrm. body weight, the urinary excretion of lime was 0·3 per cent. of the total output, and the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ was $\frac{1}{2·7}$. At the end of that period the patient was given daily exposures to radiations from a mercury vapour quartz lamp and during the second week of this treatment the daily retentions

of CaO and P_2O_5 were found to have increased respectively to 0·25 grm. and 0·22 grm. per kgrm. body weight. The output of lime in the urine increased to 3·7 per cent. of the total output and the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ became $\frac{4·7}{1}$. Healing was first noted radiographically at the end of this period, that is, the end of the second week on treatment.

Case 2. D. B., æt. 6 months. For four weeks there was no evidence of healing in the radiograms. The daily retentions of CaO and P_2O_5 were each ·64 grm. per kgrm. body weight Radiostol, 3 minims three times daily, was then given. During the second week of treatment the daily retentions of CaO and P_2O_5 were increased respectively to 0·10 and 0·08 grm. per kgrm. body weight. The urinary output of lime increased from ·4 per cent. to 2·6 per cent. of the total output and the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ which was $\frac{1}{1·6}$ during the first period, became $\frac{4·4}{1}$

Case 3. J. P., æt. $1\frac{5}{12}$ years. Weekly radiograms were taken for a period of three weeks before patient was admitted to hospital. There being no evidence of healing, the child was admitted to hospital and a metabolic study carried out which showed that the daily retentions of CaO and of P_2O_5 were each ·07 grm. per kgrm. body weight. The urinary output of CaO was 0·4 per cent. of the total output and the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ was $\frac{2}{1}$. A radiogram at the end of this period showed definite healing.

Case 4. H. W., æt. $1\frac{0}{12}$ years. Radiograms taken for four weeks before admission to hospital showed no evidence of healing. The patient was then admitted to hospital and at the end of two weeks' residence in the ward a suspicion of healing was noted in the radiographic picture. A metabolism study made at this time showed that the daily retentions of CaO and P_2O_5 were respectively ·05 grm. and ·08 grm. per kgrm. body weight. The urinary output of lime was 0·8 per cent. of the total output and the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ was $\frac{1}{3·1}$. A radiogram taken at the end of this period showed definite healing.

Case 5. D. B., æt. $3\frac{10}{12}$ years. For three weeks before admission there was no radiographic evidence of healing. After one week in the ward slight healing was noted. During the second week in hospital a metabolic study was made. The daily retentions of CaO and P_2O_5 were each 0·13 grm. per kgrm. body weight. The output of CaO in the urine was 1·9 per cent. of the total output, the ratio $\frac{P_2O_5 \text{ in urine}}{P_2O_5 \text{ in fæces}}$ was $\frac{2·4}{1}$. Further healing was noted in the radiogram taken at the end of the study.

Discussion.

The normal daily retention of lime in young children varies from about 0·06 to 0·12 grm. per kgrm. body weight. By far the greater part of the lime excreted is eliminated in the fæces, only a very small percentage (1 to 2 per cent.) being found in the urine. The retention of P_2O_5 is approximately the same as that of lime. The mode of excretion, however, is different. About 40 per cent. of the total output of P_2O_5 is excreted by the kidneys and about 60 per cent. is found in the fæces (Telfer).

Of the cases recorded above it will be seen that in the two patients where the metabolism studies were made during the active stage of the disease the retentions of Ca0 and P_2O_5 were below normal, the urinary output of lime was also low and the greater proportion of the phosphorus was eliminated in the fæces. After seven days' treatment by irradiation or the administration of radiostol, there resulted a marked increase in the retentions of both Ca0 and P_2O_5, the urinary output of lime was also increased and the larger proportion of phosphorus left *via* the kidneys.

Of the three examples of spontaneously healing rickets, Case 3, where the first radiographic evidence of healing was noted at the end of the metabolic study, had a low but normal retention of CaO and P_2O_5, while Case 5, where the first radiographic evidence of healing was noted before the metabolic study commenced, had a retention of CaO and P_2O_5 exceeding the upper limit of normality. Only the latter case, which showed the most advanced healing, presented a normal percentage output of lime in the urine. In the other two cases the urinary output of lime resembled that met with during the active stage of the disease. It will thus be seen that the retention of lime increases from a low normal retention in the case of earliest healing to a retention slightly above normal in the case of more advanced healing. It would appear probable from these results that in spontaneous healing a slight increase occurs in the retentions of CaO and P_2O_5 before radiological evidence of healing and that with the advance of healing noted in the radiographic picture a further gradual increase occurs.

It is interesting to contrast the results obtained in spontaneously healing rickets with those obtained in the treated cases. In the treated cases, there occurred a marked increase in the retentions of CaO and P_2O_5 during the week preceding the first radiographic appearance of healing. The increase in the urinary output of lime was more marked in the treated cases as was also the change in the mode of excretion of P_2O_5. This early marked change in the mineral metabolism in treated cases is comparable to the increase noted in the serum phosphorus in treated rickets before X-ray evidence of healing, and is probably to be attributed to the greater rapidity with which healing takes place when efficient treatment is given.

Conclusions.

The following conclusions seem to be justified in view of the results of the above described experiments carried out in cases of rickets to determine the relative value of various methods in arriving at a decision as to the stage of the disease.

1. Isolated observations on the inorganic phosphorus content of the blood serum are of no practical value because figures obtained from such observations in early healing often fall within the limits of those of the active stage. The same objection applies to the use of the figure representing the product of the phosphorus and calcium contents (mgrm. per 100 c.cm.).

2. Serial observations on the serum phosphorus over a period of two to three weeks are of assistance only when the disease is healing rapidly, as, for example, when active treatment is being employed.

3. A determination of the calcium balance is the most reliable means of arriving at a decision. The objection to this method is the time and labour involved, as after the metabolic study which extends over seven days is finished, a further week or ten days is required before the necessary analyses can be completed.

4. Radiograms taken over a period of three weeks are on the whole a fairly reliable means of determining the phase of the disorder, and they involve much less trouble, though they may fail to show such an early stage of healing as can be demonstrated by the calcium balance estimations.

5. Whichever method is used, a period of about three weeks is necessary to arrive at a satisfactory decision. Also it is to be remembered that if the three weeks' observations are made while the case is an out-patient, the results of these observations may indicate an active stage, and yet because of change in environment healing may be evident very shortly after the patient is admitted to hospital for investigation of the value of treatment. This happened in three of the cases recorded above. It is therefore essential that the observations be made while the patient is in the ward where all conditions can be controlled.

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ENURESIS IN HOSPITAL PRACTICE.

BY

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Enuresis in the children of families compelled by financial circumstances to live in small crowded homes, presents a problem of both clinical and sociological interest. Apart from the mental suffering of the patient, the discomfort imposed on those who share a bed with him, the mother's difficulty in keeping clothes and bedding clean with her inadequate facilities, and the disturbance caused in school to the teacher and the class, are worthy of consideration. The unpopularity of such a child at home and at school, and the continued struggle of the mother and teacher to cope with this additional burden, cannot but produce an atmosphere of nervous tension which is detrimental to the child.

Five per cent. of the total number of children attending the Children's Outpatient section of the London Hospital in one year suffered from enuresis. A study of sixty cases was made to discover any common factor in its incidence, and to attempt to obtain a quicker response to treatment by simple psychological methods in conjunction with the use of belladonna, than is usually obtained with either form of treatment separately. All factors in the treatment were made as simple as possible to ensure their practicability in the homes of such patients. Owing to the relatively small number of cases in the series it is realized that the percentage quoted in the following paragraphs may be unduly high. Among these cases were 23 boys and 37 girls, whose ages at their first attendances were between 5 and 8 years in 56·6 per cent. of the total, that is, during the period of the second dentition as noted by Still[1] in 60 per cent. of his cases. Children over 9 years of age formed 15 per cent. of the series, and the remaining 28·4 per cent. were children between 3 and 5 years old.

In 41·6 per cent. of cases the enuresis dated from infancy, and in 58·4 per cent. the onset occurred after control of micturition had been established for periods varying from 1 month to 7 years. A family history of enuresis was found in 56·6 per cent., and in two cases it could be traced to the grandparents. Grover[2] in 1918 found a family history in 56 per cent. of a series of 200 cases. A rheumatic history was given in 13 per cent. of the total cases, as compared with 11 out of the 200 cases (5·5 per cent.) studied by Still. Griffith and Mitchell[3] obtained such histories, and Holt[4] noted the association of enuresis with chorea. Six cases dated from an attack of measles. Four cases originated in severe frights. One started after a fall from the deck of a steamer, and another after a fall into a barrel of tar. The third case was that of a child liable from infancy to attacks of asthma, who had a severe bicycle accident, after which the asthma entirely cleared up, but constant diurnal and nocturnal

enuresis developed. Ninety-five per cent. of all cases had a history of previous illness; measles in 88·3 per cent., and chicken-pox and whooping-cough in 30 per cent. and 23 per cent. of cases respectively.

The prominent symptoms in this series of cases were anorexia (58·3 per cent.), restless sleep, insomnia, night terrors or sleep walking (48·3 per cent.), constipation (33·3 per cent.) and headache (13·3 per cent.). Masturbation, deep sleep, diarrhœa and vomiting, in this order of frequency, were far less common. A complete physical examination was made of each child. In 48·3 per cent. of cases no abnormality of any kind was found, but the majority had varying degrees of general debility; 23·3 per cent. had enlarged tonsils and adenoids, 8·3 per cent. had threadworms, and a similar proportion had cervical adenitis. Dental caries and rickets each occurred in 3·3 per cent. of cases. Phimosis was present in only one case in the series. A routine examination of the urine was made in each case and the deposit examined. Crystals of calcium oxalate and of uric acid were found, but in the majority of cases no abnormality of any kind was detected.

The cases were classified as follows:—

Group I. Day only (5 per cent.).—Still gives 4 per cent. of his series as belonging to this group, Holt 1·5 per cent., and Ostheimer and Levi[5] 2·2 per cent. In the present series all the patients in this group were girls of about 6 years of age. The enuresis occurred more than once daily, quite irregularly and with no definite relationship to falling asleep or to absorbing occupation in school or at play. No history of nocturnal enuresis was obtained. One case dated from infancy, the others were of eight months' duration only.

Group II. Night only (30 per cent.).—Holt's series includes 34 per cent. of cases in this group, Still finding 52 per cent. and Ostheimer and Levi 58·8 per cent. incident in their respective series. There were eight boys and ten girls in the present 30 per cent. of cases, eight of the children being troubled from infancy and the rest having the onset after control had been established for periods varying from one month to four years in duration. In two cases only was there abnormally deep sleep; the majority slept restlessly and with frequent night terrors.

Group III. Day and night (55 per cent.)—Holt's percentage in this group is 64 per cent., Still giving 55 per cent., and Ostheimer and Levi 39 per cent. In the present series there were eleven boys and twenty-two girls in this group. Enuresis occurred once by day and once by night in 54·6 per cent. of these children. In 30·3 per cent. it occurred more than once by day, and in 15·1 per cent. in this group it occurred more than once by night. In nearly two-thirds of these cases enuresis began after control of micturition had definitely been established.

Group IV. With incontinence of fæces (10 per cent.).—Incontinence of fæces, in addition to enuresis, was found in four boys and two girls, between the ages of six and ten years. In two instances both incontinence and enuresis dated from infancy, while the others started from two months to seven years after the establishment of control over the sphincters. Two boys had diurnal enuresis only. In one of them incontinence occurred two or three times

daily, while in the other it occurred once only; but in neither was there enuresis or incontience by night. A third boy had nocturnal enuresis only, and incontinence of fæces once each night. The cases having diurnal and nocturnal enuresis had incontinence of fæces only by day. A family history of enuresis and incontinence was obtained, and two cases gave a definite rheumatic history. Anorexia, insomnia with night terrors, sleep walking, and headache were the symptoms discovered, and the only physical signs found were enlarged tonsils in two cases.

An attempt was made to estimate the temperament of each child and to discover the reaction of the child to the home, and his demeanour at school. 66 per cent. were nervously unstable children, but bright and responsive; 23·3 per cent. were shy, phlegmatic children making contact with them more difficult; 10 per cent. were unstable, unresponsive children, or of poor mental ability. Definite incompatibility with the home or the mother was found in 35 per cent. of all cases.

Treatment.

All factors in the treatment were made as simple as possible for the mentality of the child and mother, for the home conditions precluded many methods advised by authorities on the subject. Each case was approached by three ways—the child, the mother and the doctor—all leading to the restoration of the child's self-confidence and subsequent control of micturition.

The child was assured he was neither naughty nor dirty, and that he was certainly going to get well if he earnestly wished it; that his mother and the doctor were helping him, but that he was himself the most important factor and could best help himself by doing as they advised. School was excused children with diurnal enuresis.

The mother was assured that her home problems were understood, and her fears about the child allayed. The alliance between the child, mother and doctor was emphasized and a hopeful outlook taken, assuming that the following plan was carried out.

1. Regular weekly attendance for a considerable time and regular administration of the medicine.

2. Never allow the child to be worried, scolded or punished (owing to their known deleterious effect). Pleasure should be shown at each improvement.

3. *Diet.*—(To secure the best physiological conditions for the cessation of enuresis and as a suggestive agent.).

(*a*) No tea, coffee, cocoa, soups, broths, or meat extracts (owing to their diuretic effects).

(*b*) No more than four small teacups of milk, milk and water or water in twenty-four hours. (This is approximately 16 oz. and should meet physiological requirements.)

(*c*) No drink after 5 p.m. Slices of lemon or orange may be sucked whenever the child is thirsty.

(*d*) No salt fish or highly seasoned food (to prevent thirst).

(*e*) Avoid heavy puddings, many potatoes, etc. (to prevent the formation of big fæcal masses in the rectum by night).

4. *Bed.*—(*a*) The child should go to bed early (adequate sleep being essential for these nervously unstable children). Sharing a room or bed, or sleeping in the living-room, often makes this difficult.

(*b*) The child should sleep on his side. A roller towel tied with a knot in the middle of the back should ensure this. Raising the foot of the bed for an indefinite period is not found practicable in crowded homes.

(*c*) Use light bedclothes and a hard mattress—alteration of either or both is often impossible in many of these families.

5. *Micturition.*—The child must pass water at regular intervals and at the same time each day, e.g., on waking, before meals, on going to bed and when the parents go to bed. The more elaborate methods of rousing the child by alarm clock at every hour, or once or twice during the night and early morning, are impracticable in the crowded homes of working people.

The doctor's share in the alliance consisted in the correction of any local irritation, e.g., urine, constipation, threadworms, the prescription of drugs, and also the cultivation of a friendly relationship with both child and mother.

(*a*) To record the number of dry days and nights for each week, praising both mother and child for any improvement and to encourage both of them to follow the suggested scheme closely.

(*b*) To obtain the co-operation of the school teacher in helping to restore the child's self-confidence by allowing unlimited opportunity for voluntary micturition in school hours, and by avoiding scolding or punishments.

(*c*) To offer the bribe of convalescence at the sea or country after six weeks' complete control. As the majority of children were debilitated this was in fact a necessity.

Fluid intake was increased gradually after complete freedom from enuresis had been obtained for a month.

Tincture of belladonna was given beginning with 5 min., t.d.s., and increasing by weekly increments of 5 min. up to 30 or 35 min., with ammonium bromide, 5 gr., t.d.s., increasing by 1 or 2 gr. each week up to 12 gr. Tincture of nux vomica in doses of 2 or 3 min. was sometimes added to the mixture. To improve the general health syrup ferri phos. co. and cod-liver oil and malt extract were given simultaneously. The dose of the belladonna and bromide mixture necessary to help the child to secure 7 dry days and 7 dry nights was maintained for a fortnight and then reduced by the same amounts as it had been increased; 5 grains of bismuth oxycarbonate with 1 minim of tincture of opium was given thrice daily before meals where incontinence of fæces occurred with enuresis.

After all belladonna had been stopped each child attended monthly for three months to ensure that no recurrence had occurred.

Results.

Sixty-five per cent. of all cases were successfully cured on this plan, and 35 per cent. improved, attaining as much as a fortnight's freedom from enuresis

but owing to irregular attendance or to discontinuing attendance they have not definitely cleared up. One third of the successful cases had a whole dry month within two months of beginning treatment. The girls responded to treatment more quickly than the boys, and it has been ascertained that over a period of nine months all these children are still free from enuresis. The time taken to obtain this result was as follows :—

Group I.—The diurnal cases cleared up in six weeks from beginning treatment.

Group II.—Half the nocturnal cases cleared up six weeks after treatment began. The remainder constitute the bulk of those cases ceasing to attend, so of them no statement can be made.

Group III.—Complete recovery in the cases with enuresis day and night was sometimes delayed as long as the eighteenth week, but either day or night was free from enuresis within two months of beginning treatment. Day was dry before night in 72·7 per cent. of the cases in this group ; night before day in 12·1 per cent., while day and night cleared simultaneously in 15·1 per cent. of these cases.

Group IV.—In the cases with incontinence of fæces, control of fæces was established after the first week in two cases, the others varying in time up to the sixth week after treatment bagan. Enuresis ceased completely after the ninth week of treatment.

It was noticed that the weekly number of dry nights decreased after drinking extra fluid in two cases. Colds, threadworms, tonsillectomy, circumcision and an operation for crushed fingers seemed responsible for delayed response to treatment. Recurrence occurred in two cases—a girl after an attack of bronchitis and a boy after a fall from a height. Both, however, recovered and up to the present are free from enuresis. Enuresis ceased completely after tonsillectomy in one case, a second child obtained complete control of micturition immediately she was admitted to the wards with pneumonia, while kindly discipline of another type—the Boy Scout movement—apparently helped one boy to recover rapidly.

Conclusions.

In this series of cases the incidence of enuresis was greater among girls than boys and the majority of cases occurred after control of micturition had been established. A family history occurred in 56·6 per cent. of cases and the symptoms of nervous instability were alone prominent. Nearly 50 per cent. of these children had no physical abnormality and only one case of phimosis occurred. Group III in which enuresis occurred by day and night was the commonest type. The children were in most cases nervously unstable, highly strung individuals, abnormally sensitive to praise or blame, which would account for the relatively large proportion of cases in which incompatibility with the home was found.

All four groups of enuresis responded relatively quickly to the combination of simple suggestive measures with the giving of belladonna as has been done in this series. Reference to the notes of thirty cases distinct from this series

shows that when no definite insistence on simple psychological treatment was made in addition to the giving of adequate doses of belladonna, or small doses of belladonna were alone given, the children remained *in statu quo* for varying periods of one to twelve months.

Freidell[6] states that of 39 cases of enuresis, 87 per cent. were successfully treated by psychic treatment of a hypodermic injection of sterile water, success or failure depending on the relative concentrations of the day and night urine, but all cases were treated by suggestion alone. In a busy outpatient department the time necessary to devote to purely psychological methods makes such treatment difficult to give.

In the present series of cases friendly co-operation between child, mother and doctor based on the scheme outlined above—a printed copy of which is given to each mother concerned—resulted in response from these children in a relatively short time. They ceased to be annoyances for whom little could be done until the age of puberty. Those who are familiar with the conditions of life of most hospital patients can gauge what this means to the mother and the family, as well as to the child himself at home and at school.

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